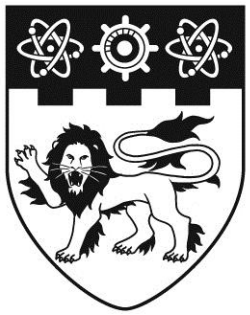

NANYANG TECHNOLOGICAL UNIVERSITY

CYCLOISOMERIZATION OF 1,*n* -ENYNE AND 1,*n* -DIYNE ESTERS AND CARBONATES TO CYCLIC COMPOUNDS VIA GOLD CATALYSIS

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SALLY

SCHOOL OF PHYSICAL AND MATHEMATICAL SCIENCES

2015

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Cycloisomerization of 1,*n*-Enyne and 1,*n*-Diyne Esters and Carbonates to the Cyclic Compounds Via Gold Catalysis

SALLY

School of Physical and Mathematical Sciences

A thesis submitted to the Nanyang Technological University
in partial fulfilment of the requirement for the degree of
Doctor of Philosophy

2015

DEDICATION

I would like to dedicate this thesis to my late grandfather, Tan Yin Kok, who inspired me to study hard and work hard for a better opportunity in life.

I would also like to dedicate this thesis to my late high school chemistry teacher, Pak Nur, without whom I would not have been inspired to major in chemistry.

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TABLE OF CONTENT

ABSTRACT

The work presented in this thesis was undertaken at the Division of Chemistry and Biological Chemistry, School of Physical and Mathematical Sciences, Nanyang Technological University, from February 2011 to December 2014 under the supervision of Assoc. Prof. Philip Wai Hong Chan.

The work of this thesis has been directed towards establishing gold-catalyzed intramolecular cycloisomerization of 1,*n*-enyne and 1,*n*-diyne carbonates and esters as synthetic strategies to cyclic compounds. This thesis is divided into three parts:

- Part I consists of Chapter I, which gives an overview of utilizing gold salts and complexes as a catalyst for the cycloisomerization of 1,*n*-enyne and 1,*n*-diyne carbonates and esters.
- Part II is directed at exploring intramolecular-based approaches for the construction of carbocycles, nitrogen heterocycles and spirocycles employing the Lewis acidic nature of gold catalysts. This part consists of 3 chapters:
    - Chapter II described an efficient gold-catalyzed synthetic route towards the preparation of structurally diverse *cis*-1,2,3,6-tetrahydropyridin-4-yl ketones and its application to the synthesis of an enantiopure analogue of the biologically active 2,3,4,4*a*,5,9*b*-hexahydroindeno[1,2-*c*]pyridine family of compounds.
    - Chapter III demonstrated the study of the cycloisomerization of 1,6,8-dienyne carbonates and esters to the formation of *cis*-cyclohepta-4,8-diene-fused pyrrolidines in the presence gold(I) catalyst. In this work, the reversible interconversion of the gold intermediates was supported by mechanistic studies.

- Chapter IV delineated gold-catalyzed tandem [2,3]-sigmatropic rearrangement/Nazarov cyclisation/6-*exo*-*dig* cyclisation/1,5-acyl migration of 1-ene-4,10-diyne esters as an efficient synthetic route to prepare a wide variety of spiro[4.5]decen-1-one and spiro[4.4]nonen-1-one.

➢ Part III consists of two chapters. Chapter VI contains the experimental data and Chapter VII includes the references related to this thesis.

PUBLICATIONS

1. "Crystal structure of (Z)-1-phenyl-3-styrylundeca-2-en-4,10-diyn-1-ol" Ganguly, R.; **Sally;** Chan, P. W. H. *Acta Cryst.* **2015**, *E71*, o64**.**
2. "Gold-Catalyzed Cycloisomerization of 1,6,8-Dienyne Carbonates and Esters to *cis*-Cyclohepta-4,8-diene-fused Pyrrolidines" Rao, W.[†]; **Sally**[†]; Berry, S. N.; Chan, P. W. H. *Chem. Eur. J.* **2014**, *20*, 13174.
3. "Gold-Catalyzed Cycloisomerization of 1,7-Enyne Esters to Structurally Diverse *cis*-1,2,3,6-Tetrahydropyridin-4-yl Ketones" Rao, W.; **Sally**; Koh, M. J.; Chan, P. W. H. *J. Org. Chem.* **2013**, *78*, 3183.

ABBREVIATIONS

Ac	acetate
Ar	aryl
BINAP	2,2'-bis(diphenylphosphino)-1,1'-binaphthyl
Bu	butyl
Bz	benzyl
Cbz	benzyloxycarbonyl
DCM	dichloromethane
DCE	1,2-dichloroethane
DFT	density functional theory
DMF	dimethylformamide
DMAP	4-(dimethylamino)pyridine
DMSO	dimethylsulfoxide
ee	enantiomeric excess
Et	ethyl
equiv	equivalent
h	hour
*i*Pr	isopropyl
IPr	1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene
LDA	lithium diisopropylamide
Me	methyl
min	minute
m.p.	melting point
NMR	nuclear magnetic resonance
*n*Hex	*n*-hexyl

*n*Pr	*n*-propyl
Nu	nucleophile
Ns	*p*-nitrophenylsulfonyl
OAc	acetate
OMe	methoxyl
Ph	phenyl
PTSA	*p*-toluenesulfonic acid
rt	room temperature
THF	tetrahydrofuran
TLC	thin layer chromatography
TMS	trimethylsilyl
Ts	*p*-methylphenylsulfonyl

Chapter I. Cycloisomerization of 1,*n*-Enyne and 1,*n*-Diyne Carbonates and Esters to Cyclic Compounds via Gold Catalysis

1.1 Introduction

Organic compounds containing the azahetero-, carbo- and spirocylic structural motif are commonly found in a myriad of natural products and synthetic molecules of potent biological activity and materials applications, selected examples of which are depicted in Figure 1.1.[1] For this reason, the field has attracted immense interest over the years, with a plethora of synthetic methods to access these cycloadducts being continuously developed.[2]

One of the most common methods for the synthesis of cyclic compounds is through the formation of a carbon-carbon bond. Generally, the formation of carbon-carbon bonds can be achieved via free radical, polar reactions and pericyclic reactions, which involve electrocyclic additions, cycloadditions and sigmatropic rearrangements.[3] While many efficient methodologies under these categories have been reported, transition metal catalysis offers an alternative advantageous method in accessing cyclic compounds chemoselectively and typically under mild reaction conditions.[4]

In recent years, the use of transition metal catalysts in the 1,*n*-enyne and 1,*n*-diyne systems have emerged as one of the most widely explored strategies, particularly in intramolecular cycloisomerization reactions due to its atom economical nature.[5] Cyclic compounds containing one or more rings are often produced in one step by utilizing this approach. Over the last 15 years, an increasing amount of attention has been given to

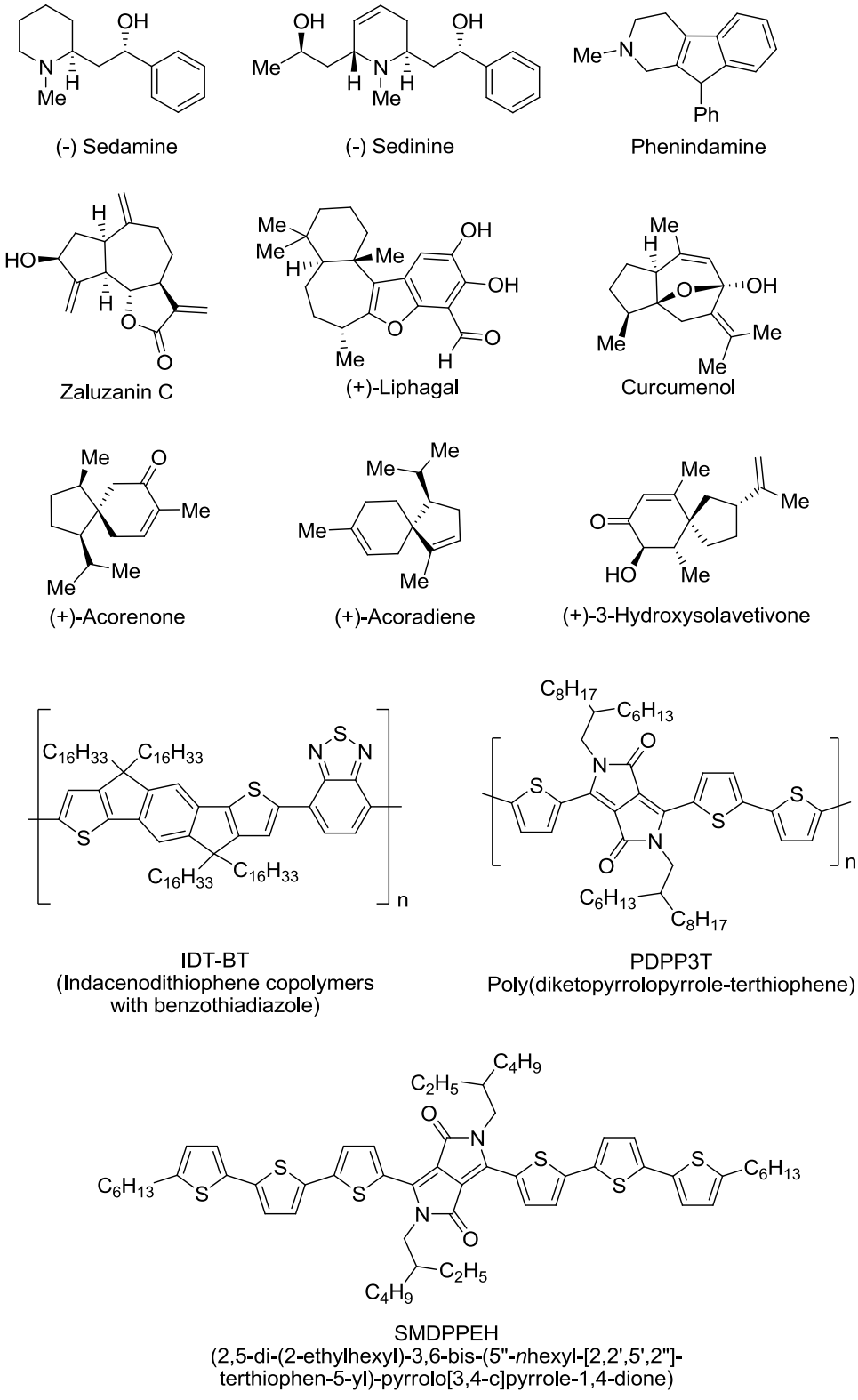


Figure 1.1 Examples of natural products and functional materials containing carbocycles, nitrogen heterocycles and spirocyclic motifs

gold due to its unique catalytic reactivities toward unsaturated π-systems of hydrocarbons not seen in other transition metals.[6]

This introduction will focus on the background of gold as an efficient catalyst as well as recent advances in the development of gold catalyzed reactions, particularly those that explore 1,*n*-enyne and 1,*n*-diyne carbonates and esters as the starting material to synthesize azaheterocycles, carbocycles and spirocyles in one step.

1.2 Lewis Acidity of Gold Complexes

The major breakthrough in the use of gold as an effective catalyst was first reported by Bond and co-workers in 1972 who demonstrated the hydrogenation of alkenes and alkynes over a supported gold catalyst.[7] This work is considered as one of the earliest milestones in the field of gold catalysis. With this discovery, the chemical view of gold changed from that of previously being an inert metal to one possessing vast reactivity potential.

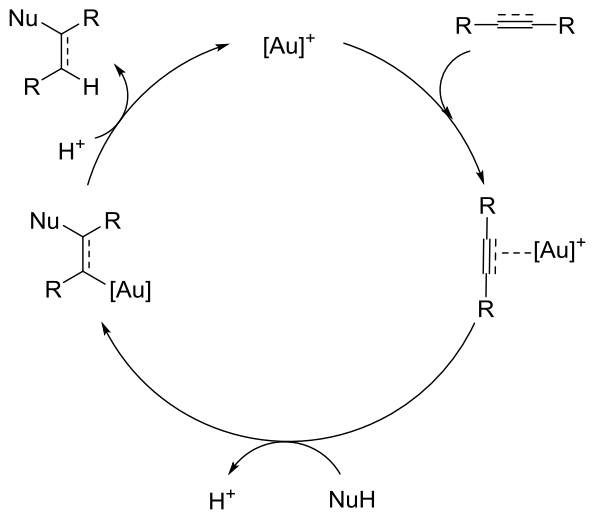
Gold (^{79}Au) is located in Period VI and Group 11 of the transition metal block in the periodic table, below copper (^{29}Cu) and silver (^{47}Ag) and between platinum (^{78}Pt) and mercury (^{80}Hg). In the early years of the development of catalysis reactions, gold was neglected as compared to other transition metals such as iron (^{26}Fe), copper (^{27}Cu), rhodium (^{45}Rh) and palladium (^{46}Pd).[8] The reason for this, other than the perceived inertness of gold, was the high price of the precious metal. However, similar to other metal catalysts, the price of gold catalysts is often due to the ligand rather than the metal itself.[9] Furthermore, gold is naturally more abundant than other industrially used

transition metals such as platinum (^{78}Pt) and rhodium (^{45}Rh) as well as recyclable and often used in a catalytic amount.

The electronic structure of gold is [Xe]4f^{14}5d^{10}6s^{1}, leading it to exist in the 3 most common oxidation states, Au(0), Au(I) and Au(III). While it is true that Au(0) is inert, salts and complexes of Au(I) and Au(III) have been shown to be proficient catalysts with a high tolerance to moisture. The catalytic property of gold salts and complexes is attributed by its high affinity for π bonds of hydrocarbons, making it a potent Lewis acid catalyst. The π-acidity can be linked with the relativistic effect which is present in metals.[10,11] This effect reaches its maximum with gold, causing the expansion of its 5d orbital and contraction of the 6s orbital to be most pronounced as compared to other metals in the periodic table. The contraction of the 6s orbital provides a lower lying unoccupied molecular orbital (LUMO) at the gold metal center which reduces the energy gap between it and the highest occupied molecular orbital (HOMO) of π bonds, thus increases its π-acidity. The expansion of the 5d orbital contributes to the destabilization of the orbital which results in the increase in back bonding of π electrons toward the gold metal center, making it viable to stabilize cationic intermediates resulting from reactions of gold with nucleophiles.[12]

The general mechanism of gold catalyzed reactions is shown in Scheme 1.1. Typically, the first step of the reaction involves the activation of π bonds of alkynes, alkenes or allenes followed by an attack by a nucleophile present in the reaction onto one of the carbon centers bearing the π bonds. In many cases, protodeauration will then take place to regenerate the gold catalyst and the product. It is noteworthy that the

oxidation state of the gold is maintained throughout this catalytic cycle. However, disproportionation of Au(I) to Au(0) and Au(III) and reduction of Au(III) to Au(I) has been reported in some cases.[13]

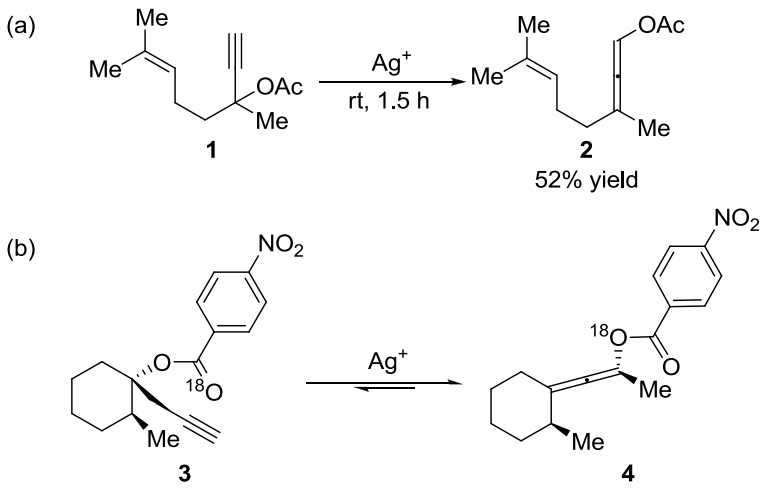


Scheme 1.1 General mechanism for gold catalyzed catalytic cycle

1.3 Propargylic Carbonates and Esters in Gold Catalysis

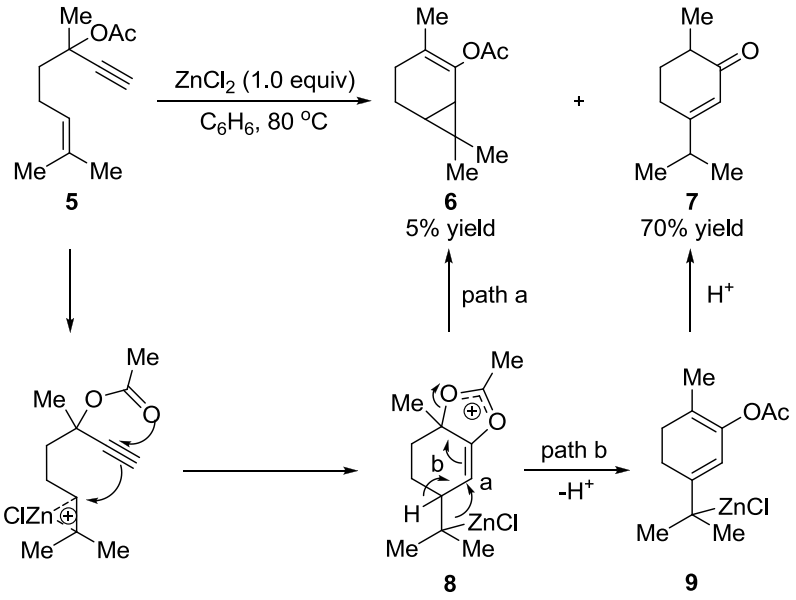
Propargylic carbonates and esters are classes of compounds which are easily accessible and possess tunable reactivities in the presence of Lewis acidic metal catalysts. In 1959, Saucy and Marbet disclosed the initial discovery of [3,3]-sigmatropic rearrangement of the acetate group in propargyl acetate **1** to give allene acetate **2** in 52% yield (Scheme 1.2a).[14] Although the rearrangement was reported, a thorough mechanistic study was only studied in 1973 by Schmid and co-workers (Scheme 1.2b).[15] In this study, an ^{18}O-labelling experiment was carried out for the rearrangement of propargyl *p*-nitrobenzoate **3** to allene *p*-nitrobenzoate **4**. The ^{18}O-labelled carbonyl oxygen atom

was shown to be retained in the product, which supported the proposed [3,3]-sigmatropic rearrangement of the propargyl ester substrate.



Scheme 1.2 Silver catalyzed [3,3]-sigmatropic rearrangement of ester group

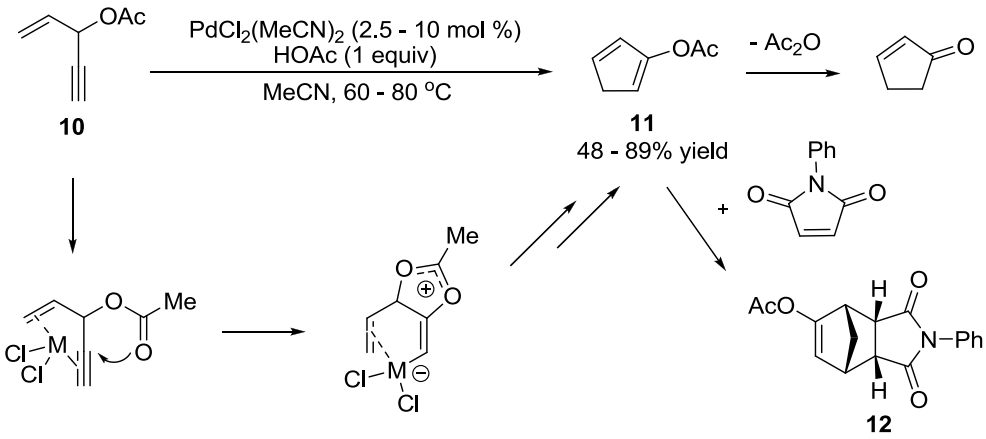
The discovery of [2,3]-sigmatropic rearrangement of propargyl esters was described by Ohloff in 1976 (Scheme 1.3).[16] In this work, the cycloisomerization of 1,6-enyne acetate **5** to 2-acetoxy-2-carene **6** in 5% yield and carvenone **7** in 70% yield was reported in the presence of a stoichiometric amount of $ZnCl_2$ as the catalyst. This transformation was proposed to proceed via activation of the alkene moiety of **5** by $ZnCl_2$ followed by cyclization and [2,3]-sigmatropic rearrangement to generate an acetoxonium ion **8**. Cyclopropanation or deprotonation then took place to form either 2-acetoxy-2-carene **6** or the diene **9** intermediate, respectively. Subsequent deacylation of the enol acetate moiety and demetallation on diene intermediate then furnished carvenone **7**. However, the [2,3]-sigmatropic rearrangement of the acetate group in the propargyl acetate remained unrecognized at this point.



Scheme 1.3 $ZnCl_2$ catalyzed cycloisomerization via [2,3]-sigmatropic rearrangement

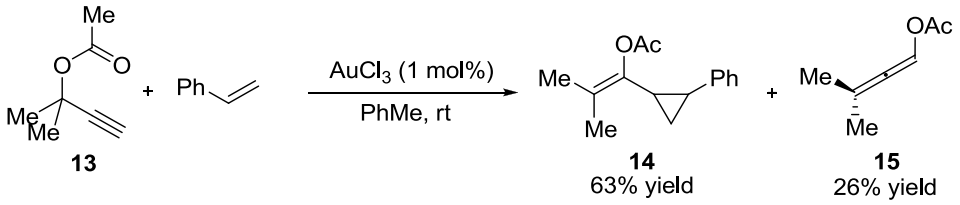
Eight years later, Rautenstrauch proposed the [2,3]-sigmatropic rearrangement in 1,4-enyne esters (Scheme 1.4).[17] In this work, both palladium and platinum catalysts were reported to effectively catalyze the cycloisomerization, which was initiated by complexation of the metal to both the alkene and the alkyne motifs of 3-acyloxy-1,4-enyne **10** that resulted in the [2,3]-sigmatropic rearrangement of the acetate group and the subsequent formation of the diene **11**. Further trapping of the diene with *N*-phenylmaleimide provided the Diels-Alder adduct **12**.

Although transition metal-catalyzed [2,3]- and [3,3]-sigmatropic rearrangement of propargylic esters were discovered almost 20 years ago, their synthetic potential were only further explored in 2003. The pioneering discovery of a gold catalyzed [3,3]-sigmatropic rearrangement of propargylic esters was reported as part of a wider study on ruthenium catalysis by Ohe, Uemura and co-workers (Scheme 1.5).[18] In the



Scheme 1.4 Pd-catalyzed cycloisomerization via [2,3]-sigmatropic rearrangement

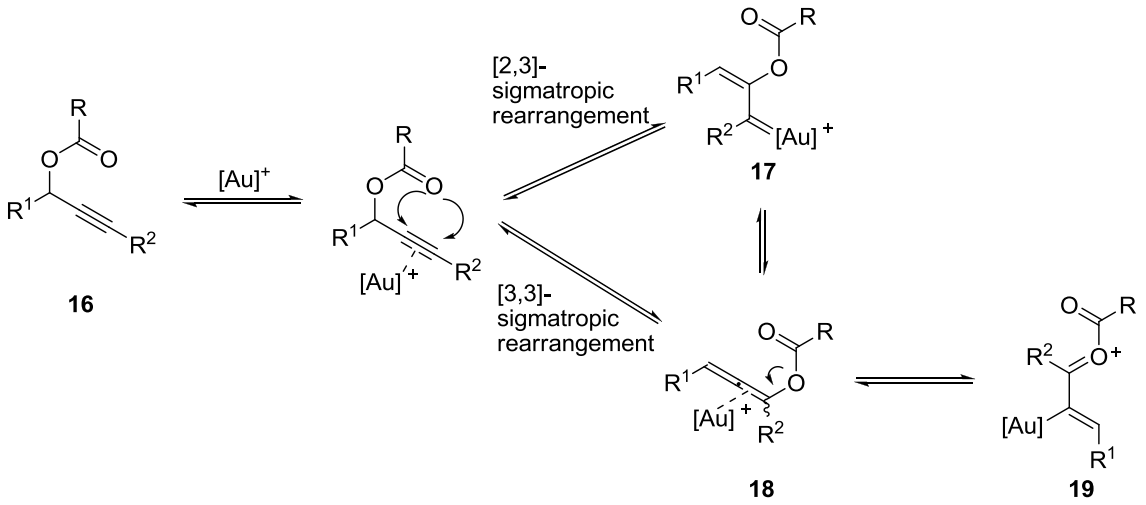
presence of styrene, propargyl acetate **13** was found to provide cyclopropane **14** as well as allene **15** in 63% and 26% yield, respectively, on treatment with 1 mol% of gold(III) chloride. The isolation of allene **15** served as evidence for the [3,3]-sigmatropic rearrangement.



Scheme 1.5 Au-catalyzed cycloisomerization via [2,3]-sigmatropic rearrangement

Following this initial discovery, the field has witnessed an exponential increase of methodologies utilizing propargyl carbonates and esters as the starting material in gold catalysis.[19,20] In general, the reactions of propargyl ester **16** has been shown to undergo [2,3]- or [3,3]-sigmatropic rearrangement to give the Au-carbenoid species **17** and Au-

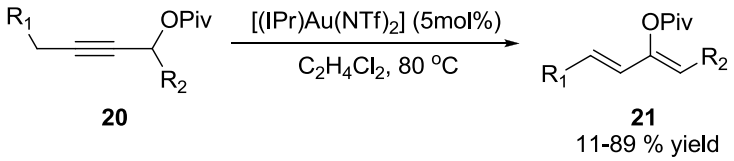
allene complex **18**, respectively (Scheme 1.6). In the case of Au-allene complex **18**, the organogold species is thought to exist in equilibrium with the α-vinyl gold oxocarbenium intermediate **19**, with the position of equilibrium largely dependent on the steric and electronic nature of the substituents.[21] In the same study by Cavallo and co-workers, an interconversion between Au-carbenoid species **17** and Au-allene complex **18** suggested a net [3,3]-sigmatropic rearrangement could be achieved via two consecutive [2,3]-sigmatropic rearrangement. Based on O^{18} labelling experiment studies conducted by Toste and co-workers in 2009, another pathway involving an equilibrium between the initial [2,3]- or [3,3]-sigmatropic rearrangement steps was also shown to be possible.[22]



Scheme 1.6 [2,3]- and [3,3]-sigmatropic rearrangement in gold catalysis

Generally, [2,3]-sigmatropic rearrangement of the ester group will occur in substrates bearing terminal and electron-poor alkynes whereas [3,3]-sigmatropic rearrangement occur in electronically unbiased internal alkynes. However a few notable exceptions have been previously reported.[23,24] It is noteworthy that other than the electronic effect,

the migration of the ester group in propargyl esters is also heavily affected by steric factors, a point that was exploited in a seminal report by Zhang and co-workers in 2008 (Scheme 1.7).[24] A series of internal alkynes **20** containing a bulky pivalate group were reported to undergo [2,3]-sigmatropic rearrangement in the presence of $(IPr)Au(NTf)_2$ (IPr = 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidine) as the catalyst to produce dienes **21** in 11-89% yield.



20 **21**
11-89 % yield

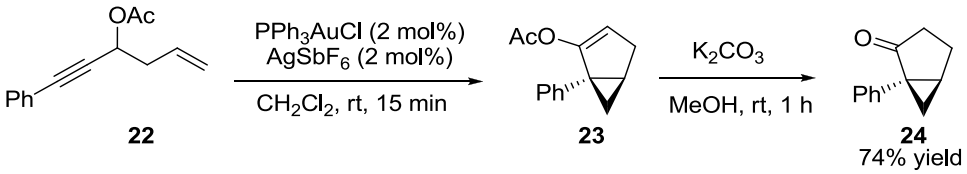
Scheme 1.7 [2,3]-sigmatropic rearrangement of bulky pivalate group catalyzed by gold

1.4 Cycloisomerization of 1,*n*-Enyne Carbonates and Esters Catalyzed by Gold

π-Acidic transition metal catalysts generally activate the alkyne moiety in 1,*n*-enyne esters whilst the alkene moiety acts as a nucleophile. Tapping on the Lewis acidic nature of gold complexes, the propensity of the ester group to undergo [2,3]- or [3,3]-sigmatropic rearrangement and the selective activation of the alkyne over alkene motif, 1,*n*-enyne esters and carbonates have risen to be a valuable and useful substrates in accessing cyclic compounds. In this context, this section will cover the pioneering and recent advances in gold catalyzed cycloisomerizations of 1,*n*-enyne carbonates and esters.

One of the earliest examples was reported by Fürstner and co-workers in 2004 (Scheme 1.8).[25] In this report, both $PtCl_2$ and $PPh_3AuCl/AgSbF_6$ were shown to effectively catalyze the cycloisomerization of 1,5-enyne acetate **22** to bicyclic pentanone

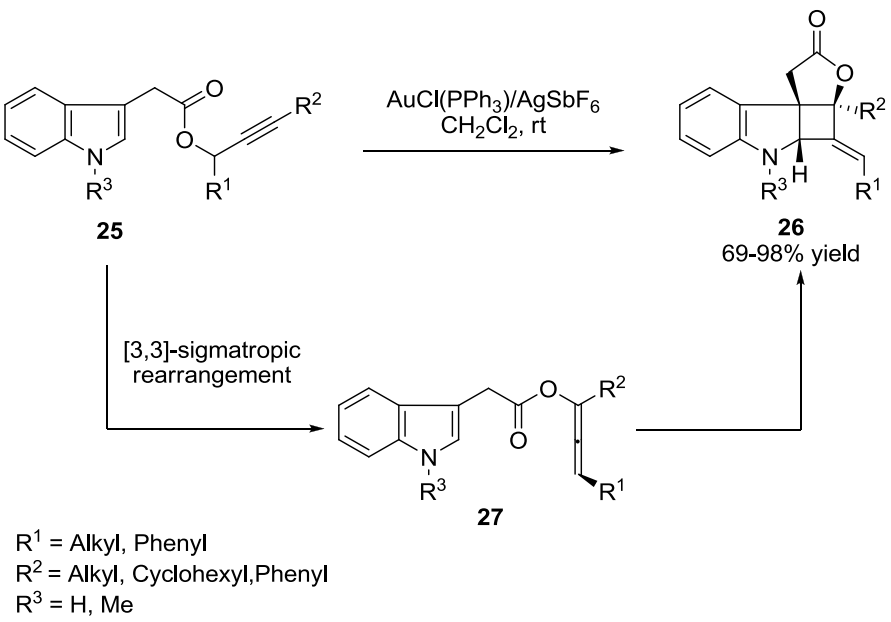
24. It was proposed that the cycloisomerization occurred via a [2,3]-sigmatropic rearrangement of the acetate group followed by trapping of the gold carbenoid intermediate by the pendant alkene moiety to furnish cyclopentene **23**. Hydrolysis of the ester group was then thought to furnish bicyclic pentanone **24** in 74% yield.



Scheme 1.8 Gold(I) catalyzed cycloisomerization of 1,5-enyne acetate

In 2005, Zhang and co-workers delineated a gold catalyzed 1,7-enyne connected through the ester moiety **25** to highly functionalized 2,3-indoline-fused cyclobutanes **26** (Scheme 1.9).[26] The transformation was thought to go through an initial [3,3]-sigmatropic rearrangement of the ester moiety in the substrate to afford allene intermediate **27**. Subsequent stepwise [2+2] cycloaddition took place to furnish the 2,3-indoline-fused cyclobutane products **26** in moderate to high yields of 69-98%. It is noteworthy that this work represent the earliest independent work on [3,3]-sigmatropic rearrangement of propargyl ester moiety in gold catalysis.

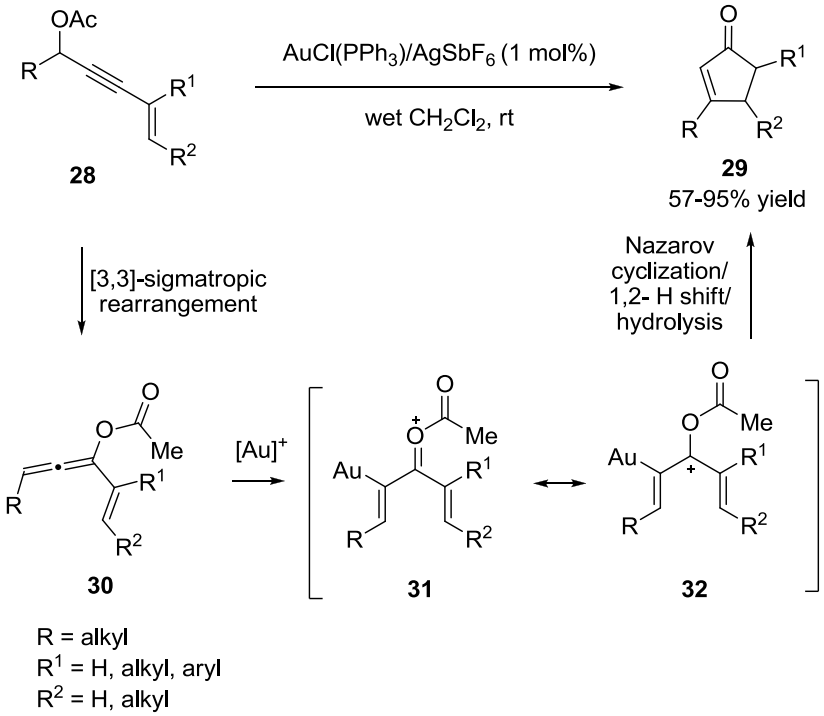
A year later, the same group described the cascade reaction of various cyclic and acyclic 1,3-enyne acetates **28** to cyclopentanones **29** in moderate to high yields of 57-95% in the presence of 1 mol% of $AuCl(PPh_3)/AgSbF_6$ (Scheme 1.10).[27] The mechanism that was proposed to involve an initial [3,3]-sigmatropic rearrangement of the acetate group to produce allene acetate **30**, which, in the presence of the Au(I) complex,



Scheme 1.9 Gold(I) catalyzed cycloisomerization of 1,7-enyne esters

further transformed to vinyl gold species **31**. Isomerization of this vinyl gold species to its gold pentadienyl-like cation species **32** that was reasoned to allow Nazarov cyclization followed by a 1,2-hydride shift to proceed, which upon subsequent hydrolysis by water present in the wet solvent, furnished cyclopentanone **29**.

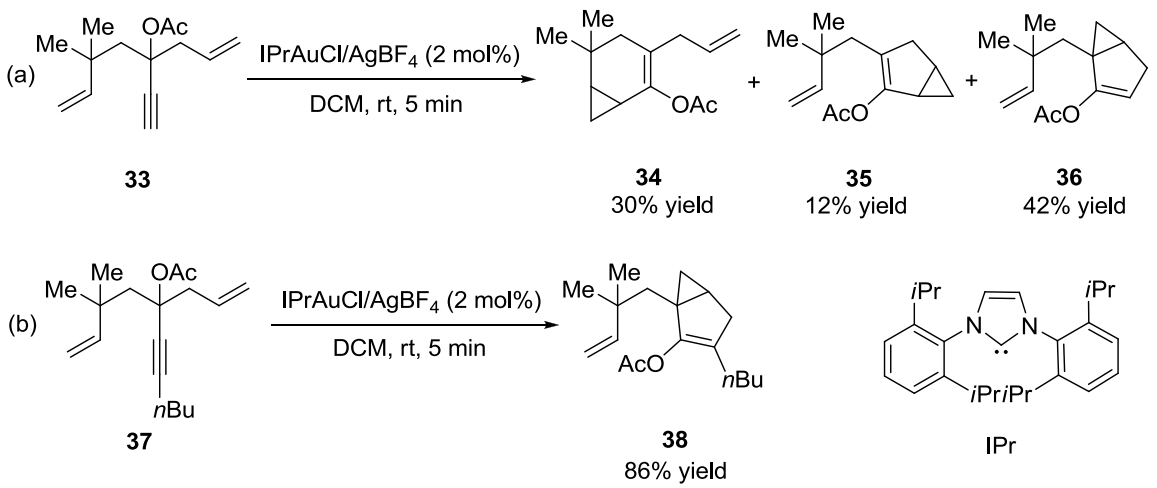
In the same year, Nolan and co-workers studied the use of gold(I) complexes containing a *N*-heterocyclic carbene (NHC) ligand. The use of IPrAuCl as the catalyst in the presence of $AgBF_4$ as the co-catalyst produced bicyclo[3.1.0]hexene **36**, which was unexpectedly detected in the product mixture along with bicyclo[4.1.0]heptene **34** and bicyclo[3.1.0] compound **35** from the cycloisomerization of 1,5-enyne acetate **33** (Scheme 1.11a).[28] This was intriguing as both **34** and **35** have been previously reported as the only products obtained in $PtCl_2$ catalyzed cycloisomerization of the same type of 1,5-



Scheme 1.10 Gold catalyzed cycloisomerization of 1,3-enyne acetate

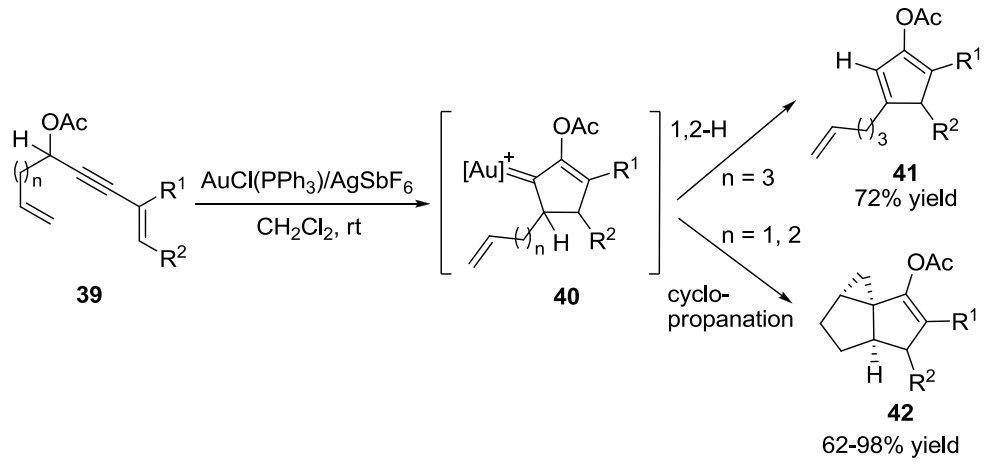
enyne acetate **33**.[29] Nolan and co-workers also showed that steric and electronic properties of both of the ancillary ligand of the NHC gold complex and the starting 1,6-enyne acetate to be important (Scheme 1.11b). In this work, a yield of 86% of the bicyclo[3.1.0]hexene **38** was obtained as the major isomer with the sterically bulky 1,5-enyne acetate **37** as the starting material. A formal 1,4-acyl migration was put forward as a possible explanation for the formation of the bicyclo[3.1.0]hexene product.

Following these works, Malacria and co-workers disclosed the analogous gold(I) catalyzed reaction of 1,5-, 1,6- and 1,7-enynyl acetates **39** bearing a tethered olefin at the propargylic position (Scheme 1.12).[30] The length of the tether was found to dictate the formation of either pentadienyl acetate **41** or tricylic compound **42**. Gold carbenoid



Scheme 1.11 NHC-Au(I) catalyzed cyclization of 1,5-enyne acetate

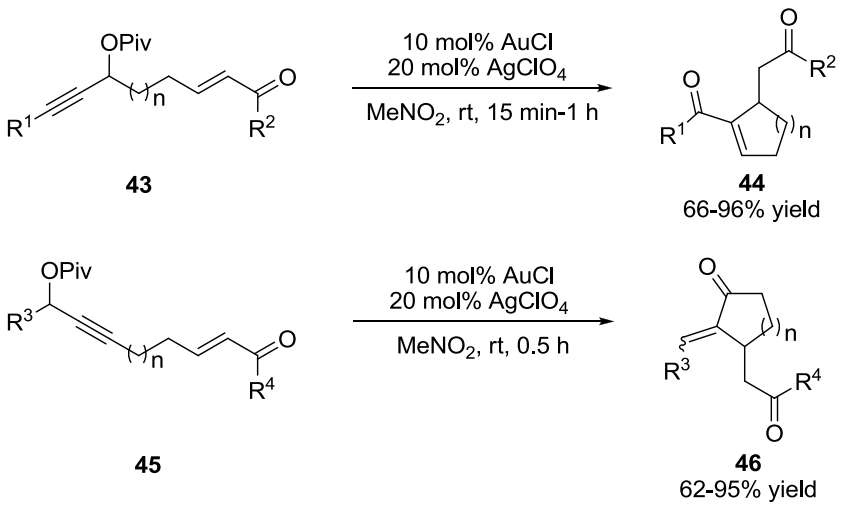
intermediate **40**, that was thought to be formed after the [3,3]-sigmatropic rearrangement step followed by Nazarov cyclization, was surmised to undergo two different mechanisms depending on the length of the tether. When n = 3, a 1,2-hydride shift was believed to take place to produce pentadienyl acetate **41** in 72% yield. On the other hand, in substrates where n = 1, 2, electrophilic cyclopropanation was reasoned to occur with



Scheme 1.12 Au(I) catalyzed cycloisomerization of 1,*n*-enynyl acetates

the olefin trapping the gold carbenoid species to furnish tricylic compound **42** in moderate to high yields of 62-98%. The use of density functional theory (DFT) calculations provided support for the proposed mechanisms.

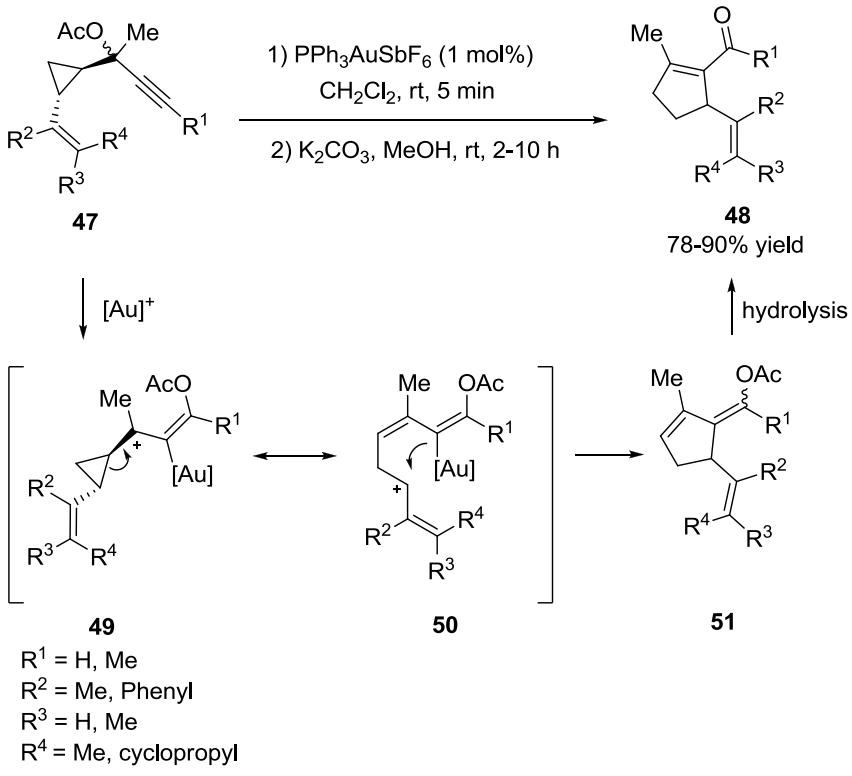
In a more recent work, Cran and co-workers delineated an interesting gold(I) catalyzed cycloisomerization of 1,6- and 1,7-enyne esters **43** and **45** to unsaturated carbocycles **44** and exocyclic enones **46**, respectively (Scheme 1.13).[31] In this work, the product divergence was achieved from the difference in the position of the ester moiety in the substrate. Mechanistically, both type of substrates were proposed to undergo an initial [3,3]-sigmatropic rearrangement of the ester moiety of the propargylic ester followed by cycloisomerization, in which the newly formed allene moiety acting as nucleophile to



Scheme 1.13 Gold catalyzed regioselective cycloisomerization of 1,6- and 1,7-enyne esters via [3,3]-sigmatropic rearrangement

attack the electrophilic α, β-unsaturated ketone unit. When 1,6- and 1,7-enyne esters **43** were employed, the unsaturated carbocyles **44** were obtained in 66-96% yield. On the other hand, the exocyclic enones **46** were obtained in 62-95% yield when 1,6- and 1,7-enyne esters **45** were subjected to a similar reaction condition. It is noteworthy that substrates bearing terminal alkyne moiety were resistant to this transformation.

1,*n*-Enynes carbonates and esters containing a strained cyclic group such as a cyclopropane have also been explored. Wang, Nevado and Goeke reported the cascade reaction of 1,6-enyne esters containing a cyclopropane moiety **47** to cyclopentenyl ketone **48** (Scheme 1.14).[32] The proposed mechanism was reported to involve a [3,3]-sigmatropic rearrangement of the propargyl ester group in the substrate to produce

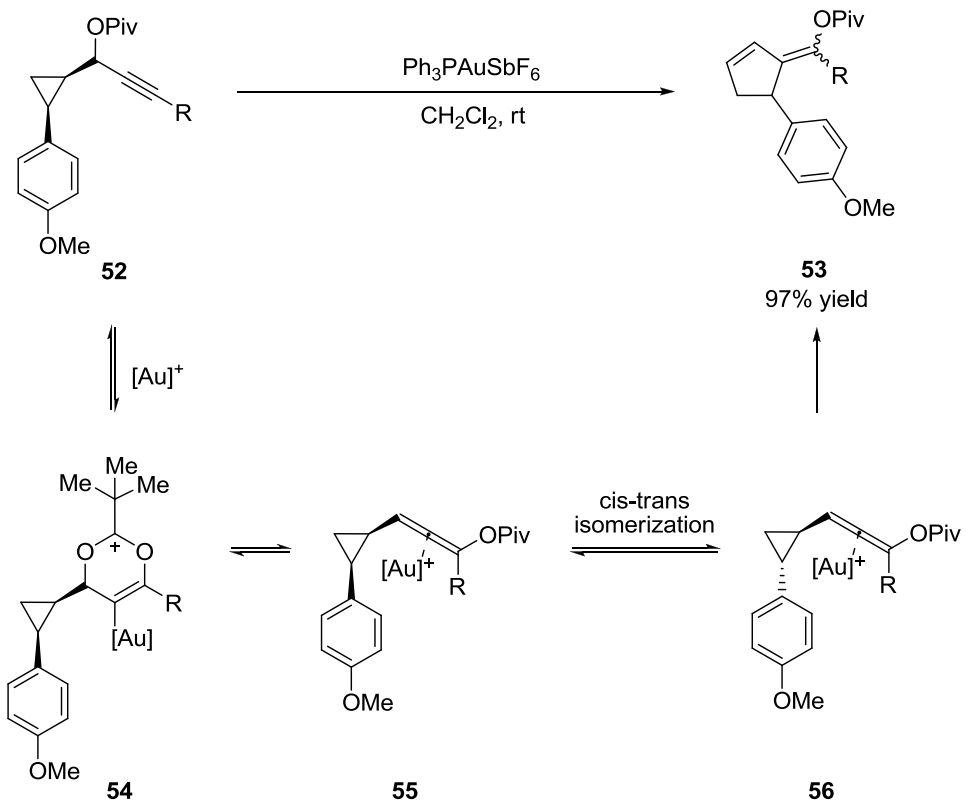


Scheme 1.14 Gold(I) catalyzed cascade reaction of propargylic esters

carbenium ion **49** followed by ring opening of the cyclopropane moiety to generate allylic cation **50**. The vinyl gold moiety then acted as a nucleophile to attack the cationic center, forming exocyclic vinyl acetate **51** as a mixture of the *cis* and *trans* isomer. Subsequent hydrolysis afforded the corresponding cyclopentenyl ketone **48**. In this report, a total of 4 examples were reported in high to excellent yields of 78-90%. Other than cyclopentenyl ketones, a few examples of cyclohexenones and cycloheptenones were also reported to be efficiently synthesized. Propargyl acetates bearing chiral centers could also be converted to the corresponding optically active cyclohexenones and cyclopentenyl ketones.

A thorough study on the mechanistic details in the rearrangement of closely related cyclopropyl adducts was subsequently reported by Toste and co-workers (Scheme 1.15).[22] Stereochemically well-defined propargyl pivalate **52** was subjected to gold(I) catalyst $Ph_3PAuSbF_6$ to explore the reversibility of the [3,3]-sigmatropic rearrangement process of the pivalate moiety. Substrate **52** was reported to undergo [3,3]-sigmatropic rearrangement to form cyclic intermediate **54** followed by ring opening to produce gold activated allene **55**. *Cis-trans* isomerization of **55** was reasoned to give higher quantity of the more stable *trans*-cyclopropane **56**, although the exact mechanistic rationale of this step remained unclear. Cyclisation via ring expansion of the *trans* isomer **56** then afforded the cyclopentane product **53**.

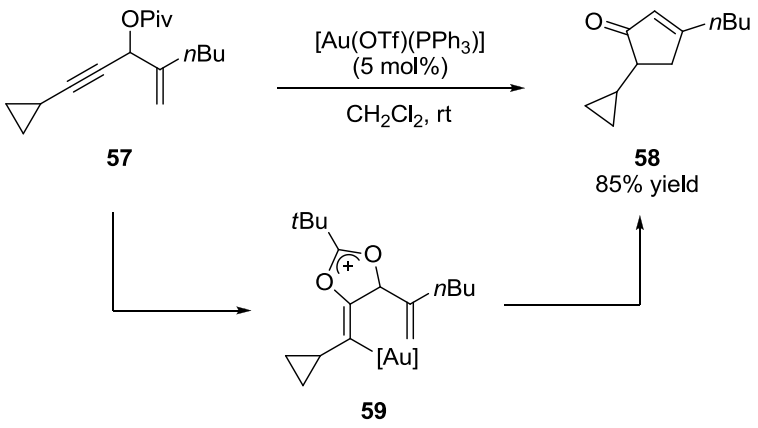
In some cases, the cyclopropane group is not involved in the reaction. One such example was reported by Toste and co-workers in the cyclization of 1,4-enyne ester **57** promoted by $Au(OTf)(PPh_3)$ to afford cyclopentenone **58** in 85% yield (Scheme 1.16).[33]



Scheme 1.15 Mechanistic study on Au(I) catalyzed cycloisomerization of **52**

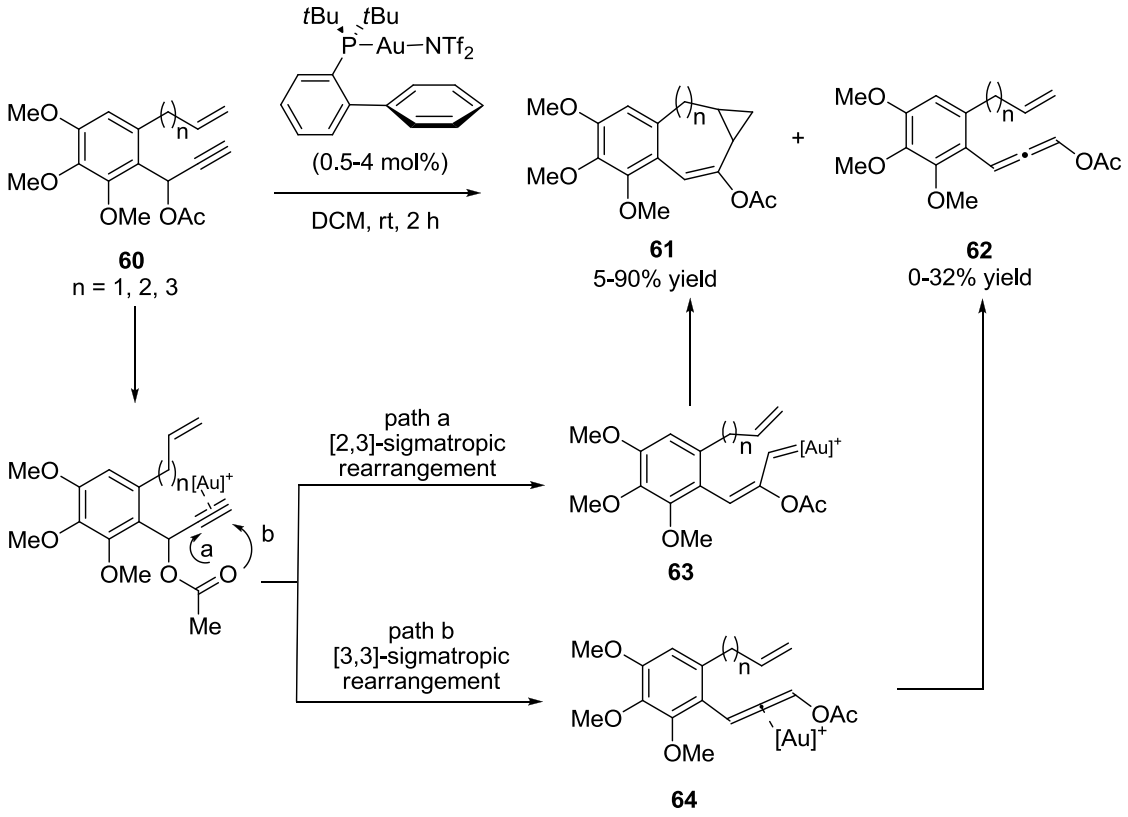
Added to this, the cyclization of 1,4-enyne acetates were studied and it was found that switching the acetate group to a pivalate group gave better product yields. The mechanism was studied a year later by De Lera and co-workers[34] via DFT calculations, which suggested the involvement of a [2,3]-sigmatropic rearrangement of the pivalate moiety to form the vinyl gold species **59**. Electrocyclization was then thought to take place to furnish cyclopentanone **58**.

Another type of 1,*n*-enyne ester that are used widely are those bearing a phenyl backbone. In 2008, Boyer and co-workers reported the cycloisomerization of 1,7- and



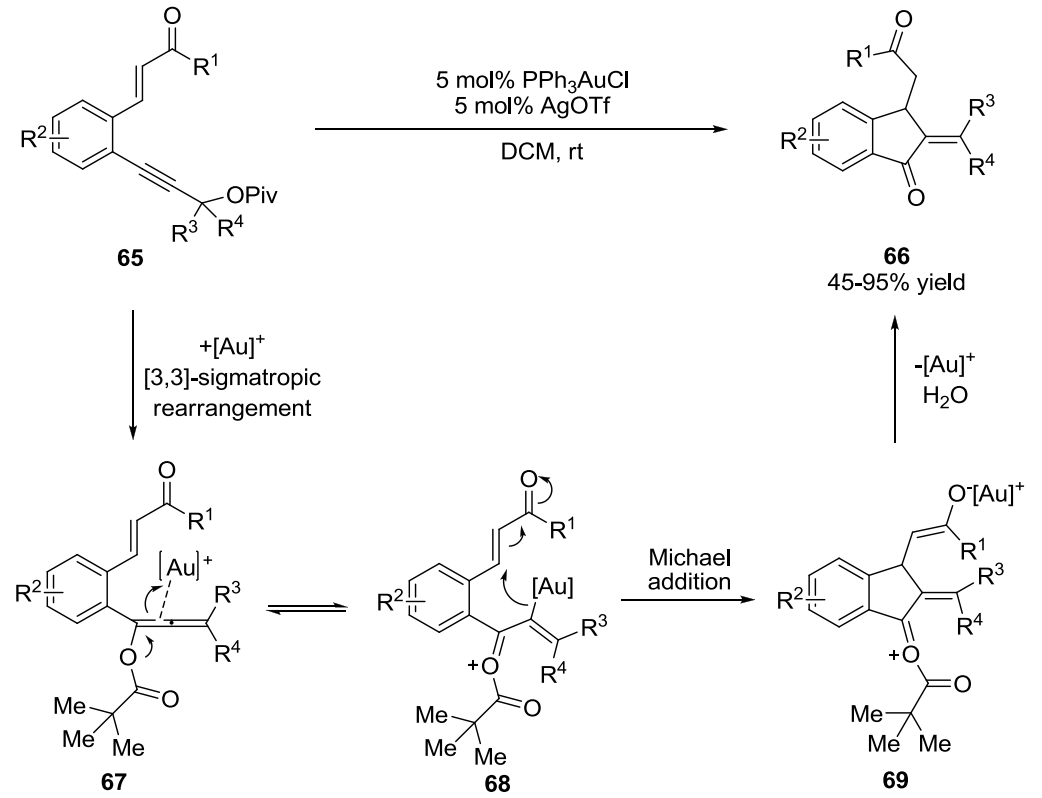
Scheme 1.16 Cycloisomerization of 1,4-enyne pivalate to cyclopentenone via a [2,3]-sigmatropic rearrangement

1,8-enyne propargylic acetates **60** in the presence of a Au(I) phosphine complex as catalyst to provide tricyclic enol ester **61** in low to high yield of 5-90% and allene acetate **62** in yields of 0-32% (Scheme 1.17).[35] The presence of allene acetate **64** as one of the products served to provide evidence of both [2,3]- and [3,3]-sigmatropic rearrangement in the same substrate. It was proposed that the [2,3]- and [3,3]-sigmatropic rearrangement of the substrate gave the gold carbenoid complex **63** and gold allene species **64**, respectively. Further transformations of these intermediates furnished the tricyclic enol ester **61** and allene acetate **62**. It was also suggested that the formation of **61** and **62** depended on the size of the ring formed. For n = 1, the substrate was thought to undergo [2,3]-sigmatropic rearrangement followed by ring closure occurred exclusively to produce **61**. On the other hand, it was believed for n = 2, 3 in the substrate, preferential [3,3]-sigmatropic rearrangement occured due to the strain of eight and nine membered ring formation and this led to a higher yield of **62**.



Scheme 1.17 Gold catalyzed cycloisomerization of 1,7- and 1,8-enynes via both [2,3]- and [3,3]-sigmatropic rearrangement pathways

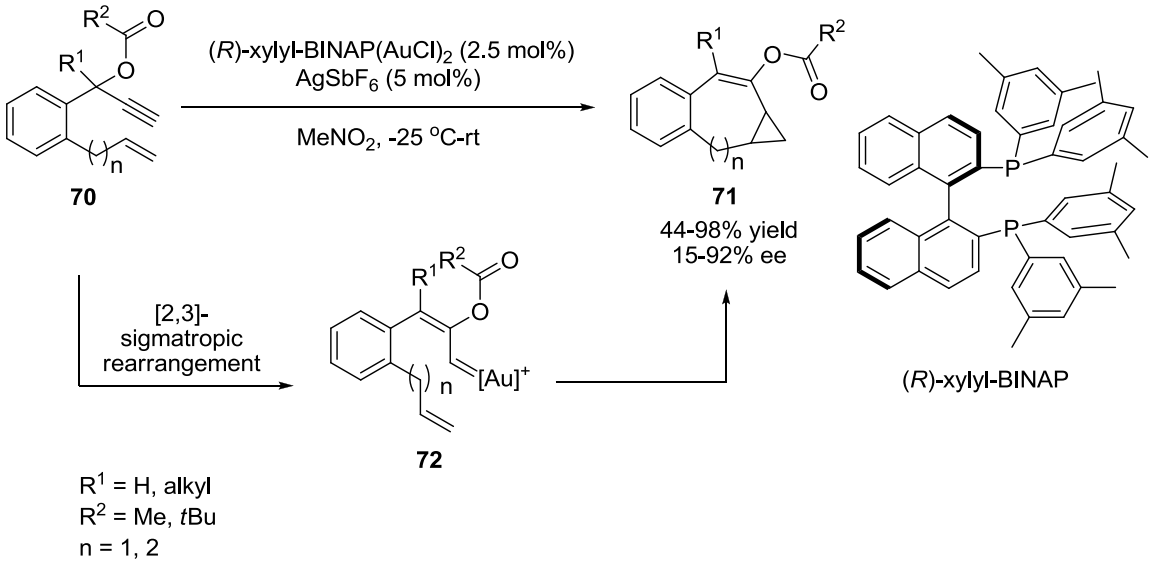
Recently, Liang and co-workers disclosed a gold catalyzed tandem reaction of 1,5-enyne ester containing phenyl backbone **65** to (*E*)-1*H*-indene-1-ones **66** in 45-95% yield (Scheme 1.18).[36] In this work, [3,3]-sigmatropic rearrangement of the propargyl ester unit was thought to take place to afford the allene intermediate **67**. This newly formed allene moiety was activated by gold(I) present in the reaction to give the putative gold intermediate **68**, which was then proposed to undergo Michael addition to give the cyclopentane intermediate **69**. Further hydrolysis took place to furnish the expected (*E*)-1*H*-indene-1-ones **66**.



R^1 = Me, Ph, *p*-ClC_6H_4, *p*-MeC_6H_4
R^2 = H, Me, F
R^3 = Me, *n*C_3H_7, *n*C_6H_{11}, Ph, *o*-ClC_6H_4, *m*-ClC_6H_4, *p*-ClC_6H_4,*o*-MeC_6H_4, *p*-MeC_6H_4, *m*-$OMeC_6H_4$
R^4 = H, Me, Et,

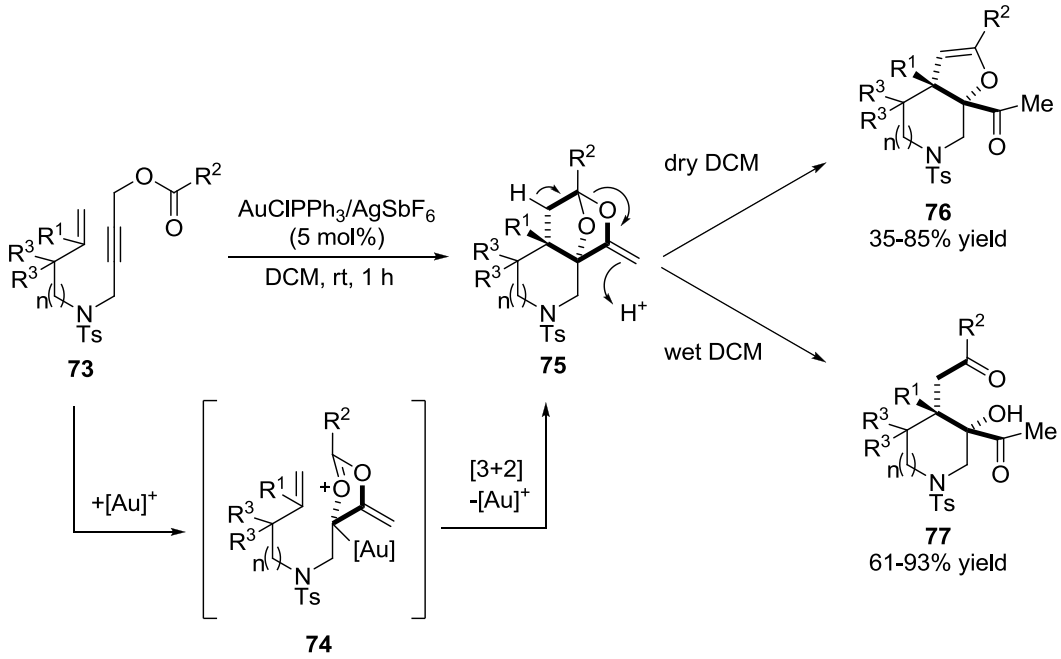
S**cheme 1.18** Gold catalyzed tandem reaction of 1,5-enyne esters

Asymmetric intramolecular synthesis involving gold as the catalyst is another important area which is being explored. In a seminal report, Toste and co-workers depicted the first gold catalyzed asymmetric formation of 7- and 8-membered rings **71** from intramolecular cyclopropanation of 1,7- and 1,8-enyne esters **70** bearing a phenyl backbone by utilizing chiral ligand (R)-xylyl-BINAP (Scheme 1.19).[37] Mechanistically, gold carbenoid intermediate **72**, formed via [2,3]-sigmatropic rearrangement, was reasoned to undergo cyclopropanation to give the cyclic products **71** in 44-98% yield and with high enantiomeric excess (ee) values of up to 92%.



Scheme 1.19 Gold catalyzed asymmetric intramolecular cyclopropanation

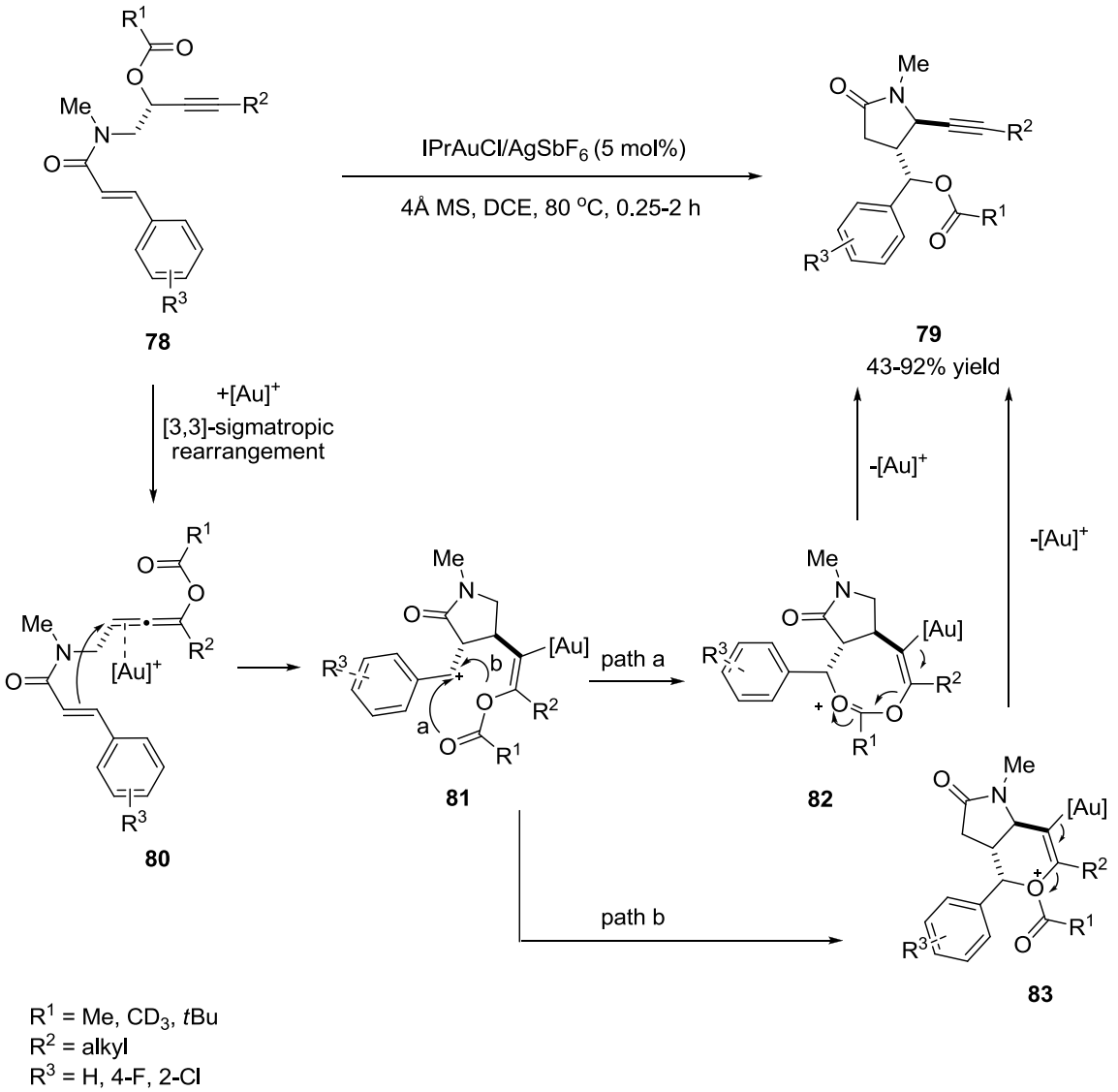
1,*n*-Enynes carbonates and esters bearing nitrogen atom have also been explored to efficiently synthesize azaheterocycles. In 2011, She and co-workers reported a gold(I) catalyzed tandem [2,3]-sigmatropic rearrangement/[3+2] cycloaddition of 1,6- and 1,7-enyne esters **73** (Scheme 1.20).[38] This transformation was proposed to involve double [2,3]-sigmatropic rearrangement to provide transition state **74** which would then undergo [3+2] cycloaddition with the alkene unit to afford bridged intermediate **75**. The substitution pattern at both R^1 and R^3 positions along with the dryness of the solvent used were shown to give rise to product divergence. When either R^1 or R^3 = Me, cyclization in dry dichloromethane (DCM) produced bicyclic adduct **76** in up to 85% yield. On the other hand, when $R^1 = R^3$ = H, cyclization in dry DCM produced the bicyclic product **76** in a low yield of 35%. Further optimization of these substrates were carried out and it was found that by utilizing wet DCM as solvent, the cyclization afforded the hydrolyzed adducts **77** in moderate to high yields of 61-93%.



Scheme 1.20 Gold(I) catalyzed tandem sigmatropic rearrangement/[3+2] cycloaddition of 1,6- and 1,7-enyne esters

Recently, Hashmi and co-workers reported the NHC-gold(I) catalyzed cycloisomerization of 1,7-enyne esters **78** to 3,4-disubstituted pyrrolidin-2-ones **79** in moderate to high yields of 43-92% (Scheme 1.21).[39] In this work, a long range 1,6-acyloxy migration step was proposed for the first time via double migration of the ester group. It was thought that the reaction proceeded by an initial [3,3]-sigmatropic rearrangement of the propargylic ester moiety to form the allene intermediate **80**. The pendant alkene moiety then acted as the nucleophile to attack the allene intermediate **80**, forming the carbocationic intermediate **81**. This carbocationic intermediate was then

proposed to be attacked by either the carbonyl oxygen or alkoxy oxygen atom in the ester moiety to give either 8-membered ring intermediate **82** or 6-membered ring intermediate **83**, as depicted in pathways a and b in Scheme 1.21, respectively. Regardless of the pathways taken, deauration of the intermediates was thought to furnish the 3,4-disubstituted pyrrolidin-2-one **79**.

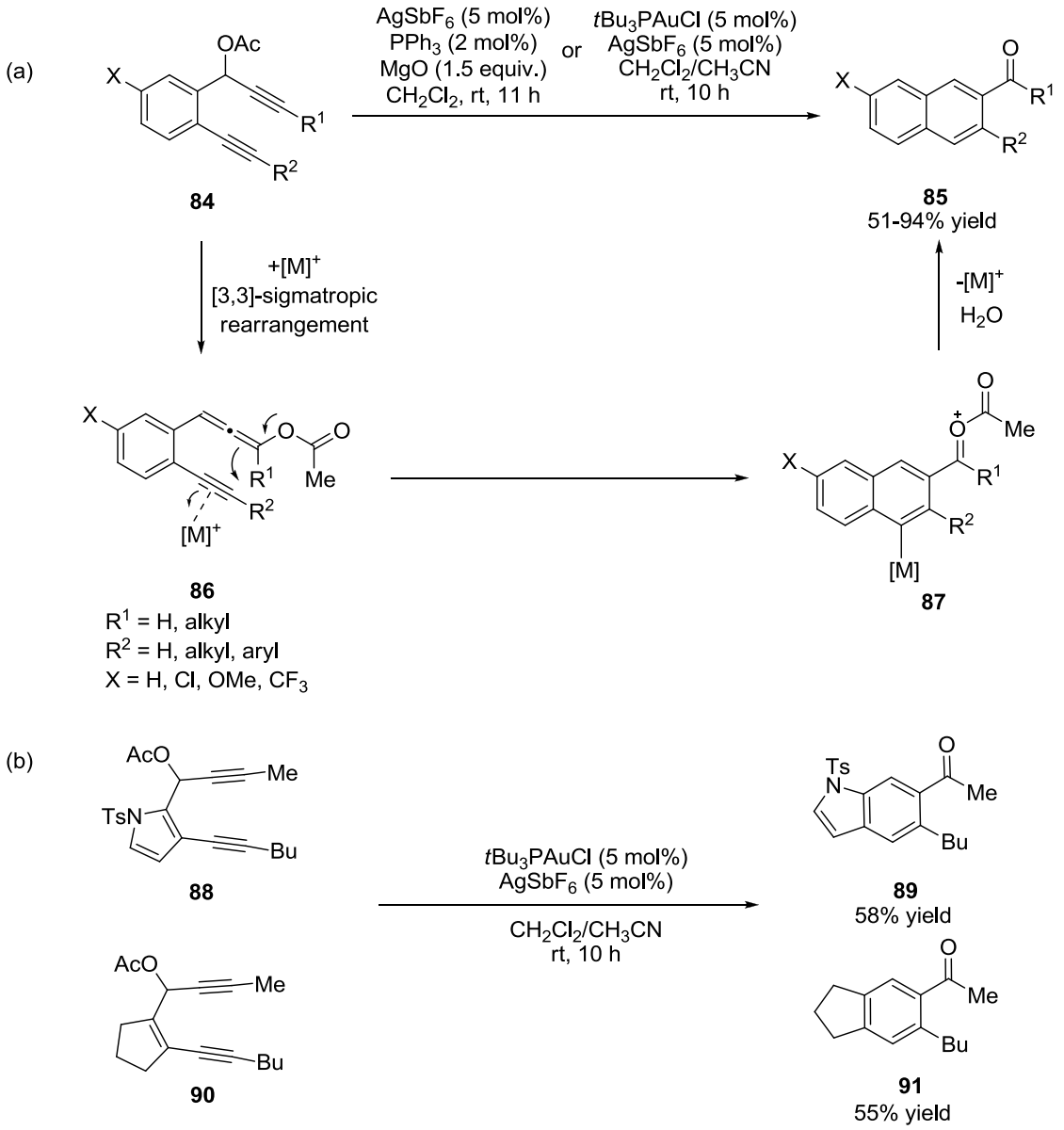


Scheme 1.21 First gold catalyzed long range 1,6-acyloxy migration in 1,7-enyne esters

1.5 Cycloisomerization of 1,*n*-Diyne Carbonates and Esters Catalyzed by Gold

Aligned with studies exploring the reactivities of 1,*n*-enyne carbonates and esters, there has also been an increasing amount of attention focused on the gold catalyzed chemistry of 1,*n*-diyne carbonates and esters. Although less well explored as compared to the 1,*n*-enyne esters, an increasing number of reports on the use of gold in catalyzing reactions with compounds bearing the 1,*n*-diyne scaffold has been witnessed in the last 10 years.[40] The difference in the chemical reactivities offered by the pendant alkyne moiety in this class of substrates has opened another useful pathway to accessing complex molecules. Recent advances in this field are discussed in this section.

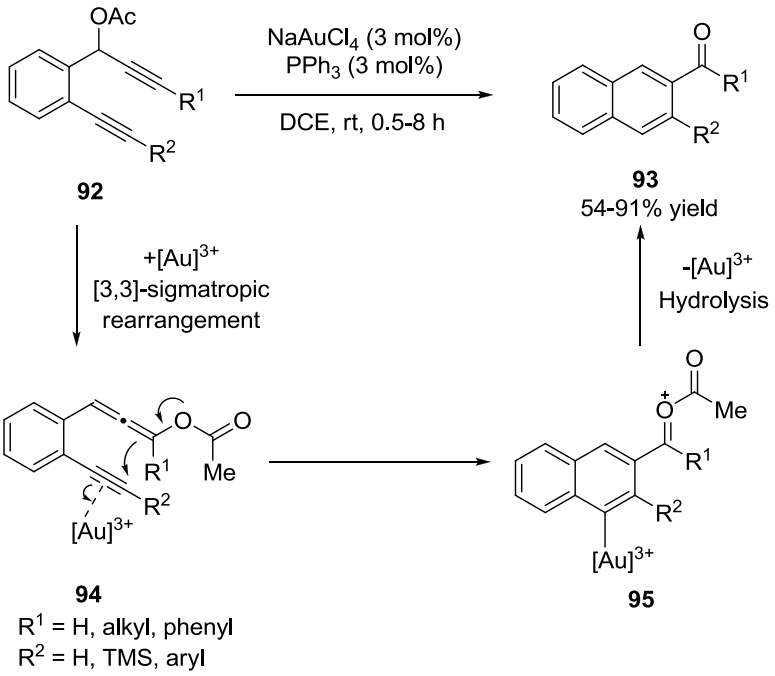
In 2006, Toste and co-workers reported a cycloisomerization of 1,6-diyne esters **84** to aryl ketones **85** (Scheme 1.22a).[41] The cycloisomerization was shown to be catalyzed by either $AgSbF_6$ or tBu$_3$PAuCl, with $AgSbF_6$ giving a better yields of 51-94% in majority of the substrates. The reaction was proposed to be initiated by [3,3]-sigmatropic rearrangement of the propargylic ester group in the presence of either Ag^+ or Au^+ to give the allenyl ester **86**. Subsequent activation of the alkyne moiety by the Lewis acidic metal catalyst triggered 6-*endo*-*dig* cycloaddition to produce the oxocarbenium cation intermediate **87**, which underwent hydrolysis to give the aryl ketone **85**. In the case of diyne **88** and **90**, it was found that these substrates could only be cyclized by tBu$_3$PAuCl to produce indole **89** and acetophenone **91** in moderate yields of 58% and 55%, respectively (Scheme 1.22b). It is noteworthy that the yield of some substrates can be increased by adding magnesium oxide as an additive in order to neutralize the acetic acid formed from hydrolysis of the acetate group.



Scheme 1.22 Silver and gold catalyzed cycloisomerization of 1,6-diyne esters

In the same year, the analogous reaction was reported by Oh and Kim (Scheme 1.23).[42] In their work, $NaAuCl_4$ in the presence of triphenylphosphine was shown to catalyze the cycloisomerization of 1,6-diyne ester **92** to aromatic ketone **93**. The mechanism was thought to involve [3,3]-sigmatropic rearrangement to give allene

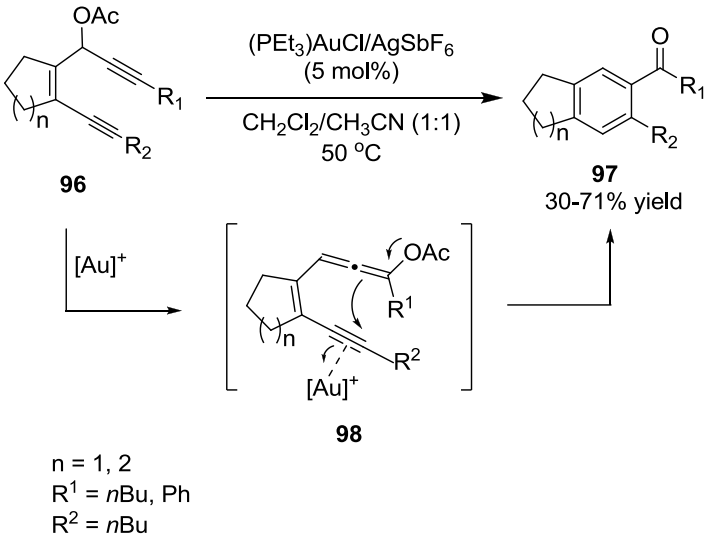
ester **94**, which was further functionalized by cyclization with the pendant alkyne moiety to furnish the oxocarbenium intermediate **95**. Hydrolysis of the intermediate gave the aromatic ketone **93** in moderate to high yields of 54-91%. Although the starting material and proposed mechanism were closely similar to the earlier report by Toste and co-workers, this approach was shown to be simpler as no co-catalyst was needed and required shorter reaction times.



Scheme 1.23 Gold(III) catalyzed cycloisomerization of 1,6-diyne esters

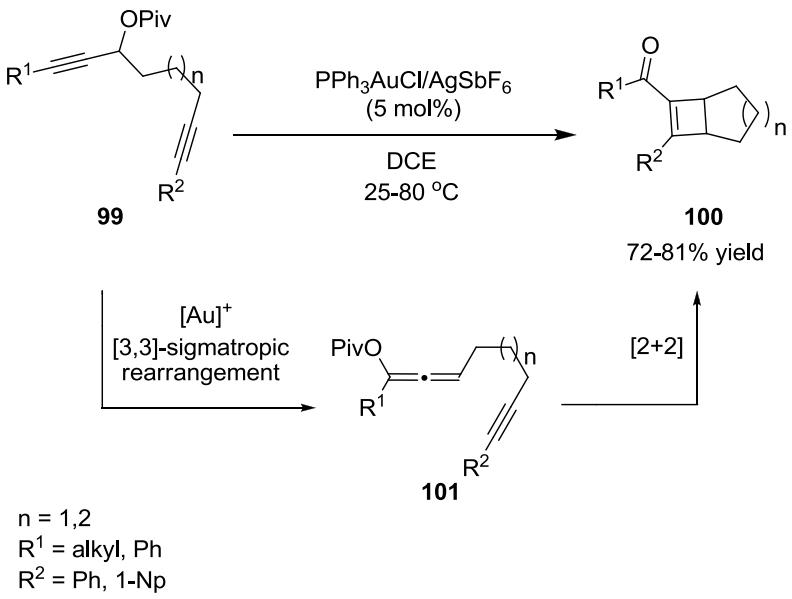
A year later, the same group reported the cycloisomerization of 1,6-diyne carbonates and esters **96** to give aryl ketones **97** in low to good yields of 30-71% (Scheme 1.24).[43] In this report, the benzene ring backbone of the diyne was replaced by a structurally less rigid cycloalkene moiety. The proposed mechanism was similar to the earlier work by the

group and that of Toste and co-workers, involving [3,3]-sigmatropic rearrangement of the propargyl ester group in the substrate to give the allene intermediate **98**. Further cyclization was thought to take place to produce the aryl ketone product **97**.



Scheme 1.24 Gold(I) catalyzed cycloisomerization of 1,6-diyne esters bearing a cycloalkene backbone

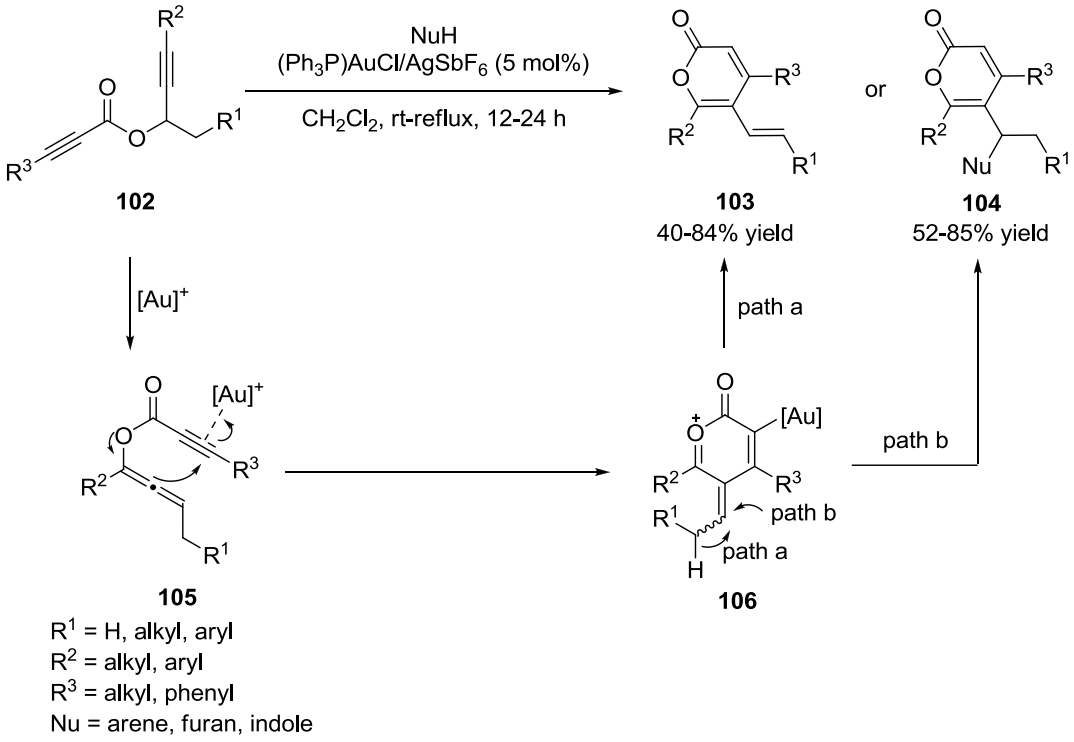
Following this work, the cycloisomerization of 1,7- and 1,8-diyne pivalates **99** into [3.2.0] and [4.2.0] bicycles **100** by utilizing $PPh_3AuCl/AgSbF_6$ as catalyst was reported by Oh and Kim (Scheme 1.25).[44] In this work, it was shown that [3,3]-sigmatropic rearrangement of the propargylic ester group in the substrate on treatment with the gold(I) catalyst provided allene pivalate **101**. Subsequent [2+2] cyclization of this newly formed adduct then furnished the [3.2.0] and [4.2.0] bicycles **100** in a good yields of 72-82%. This method provided an efficient method for the preparation of polycyclic compounds as well as an example of [2+2] cyclization of the allene and diyne moieties.



Scheme 1.25 Gold(I) catalyzed [2+ 2] cyclization of 1,7- and 1,8-diyne pivalates

Schreiber and co-workers explored the use of 1,6-diyne connected through the ester moiety, as depicted in Scheme 1.26.[45] Propargyl propiolate **102** was shown to furnish trisubstituted pyrones **103** in 40-84% yield and arene incorporated trisubtituted pyrones **104** in 52-85% yield in the presence of $PPh_3AuCl/AgSbF_6$ and a nucleophile such as arenes, furan and indole. Mechanistically, it was thought that propargyl propiolate **102** underwent [3,3]-sigmatropic rearrangement to allene ester **105**. Upon 6-*endo-dig* cyclization of this species, oxocarbenium intermediate **106** was produced**,** which allowed either a 1,2-hydride shift and demetallation to occur furnishing trisubstituted pyrones **103** or nucleophilic attack by electron rich arene to give arene incorporated trisubtituted pyrones **104**, as shown in Scheme 1.26, paths a and b, respectively.

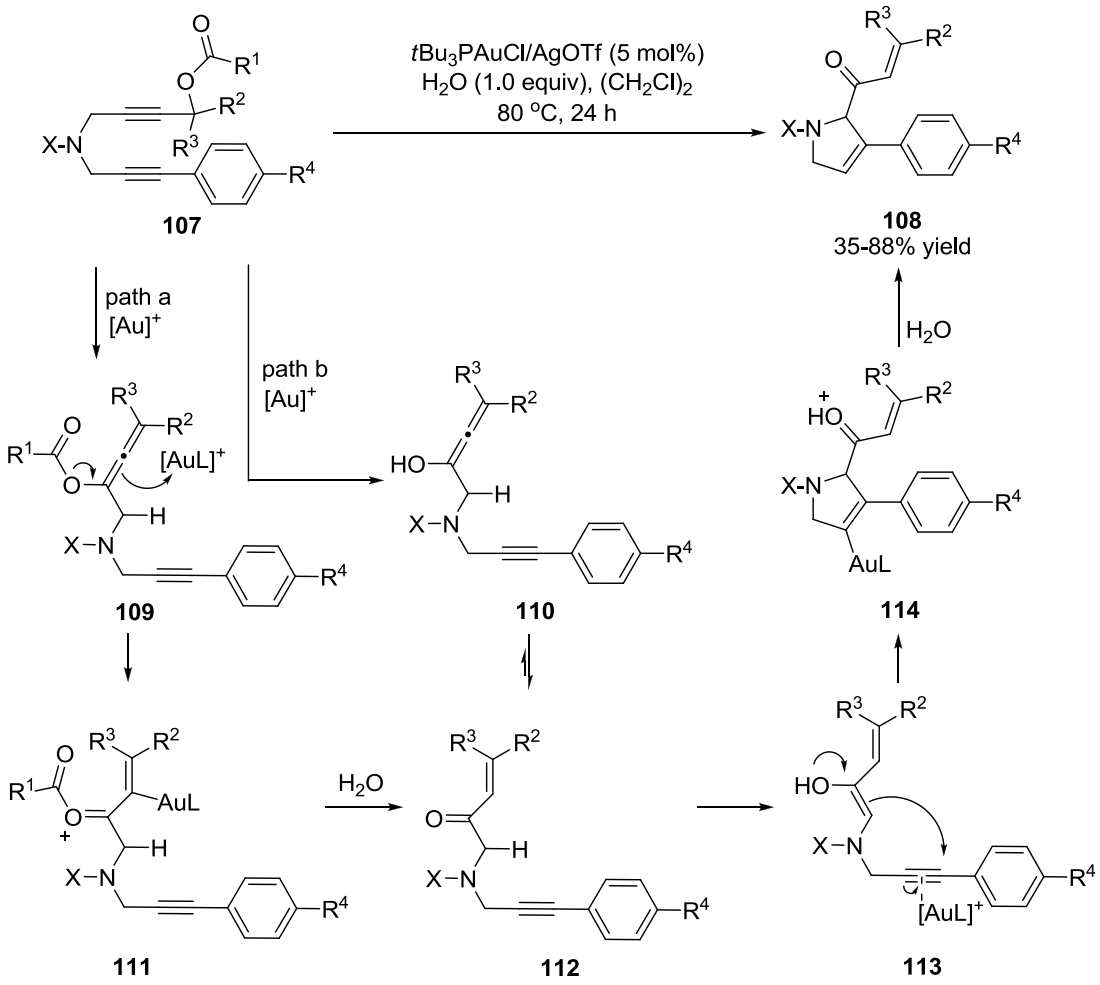
The first example of gold catalyzed cycloisomerization of 1,6-diyne esters and carbonates bearing a nitrogen atom was reported in 2011 by Shi and co-workers



Scheme 1.26 Gold(I) catalyzed cascade reaction of propargyl propiolate

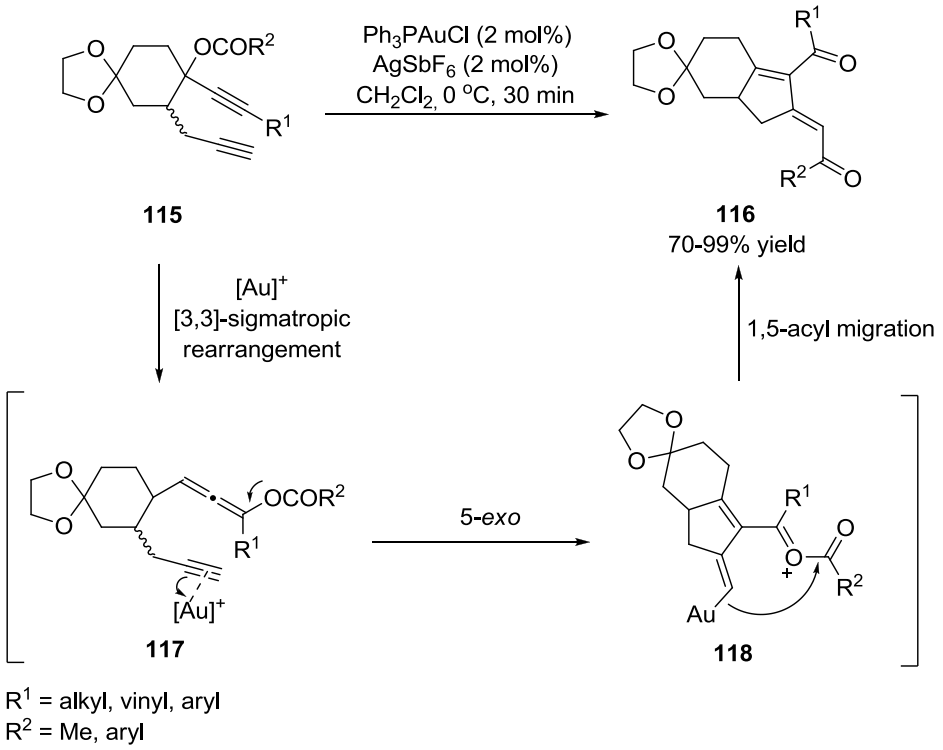
(Scheme 1.27).[46] In this work, 1,6-diyne esters **107** was cyclized into nitrogen containing five membered heterocycle **108** in low to high yields of 35-88%. It was proposed that the reaction could proceed via two possible mechanistic pathways. Pathway a involved gold catalyzed [3,3]-sigmatropic rearrangement of the propargyl ester group in the substrate to form allene intermediate **109**. Further activation by the gold(I) catalyst of the allenic moiety in the adduct then transformed it to oxonium intermediate **111**. Subsequent hydrolysis then gave the alkynyl conjugated enone **112**. The second pathway was thought to occur by Meyer-Schuster-like rearrangement of the substrate with nucleophilic attack of water on the alkyne moiety next to the ester group. This was followed by release of the AcO-group to give intermediate **110**, which upon tautomerization, afforded the alkynyl

conjugated enone **112**. The common intermediate alkynyl enone **112** could further enolize in the presence of Lewis acid to give conjugated enol **113**, which would then undergo 5-*endo-dig* cycloaddition via gold(I) activation of the alkyne moiety to give intermediate **114**. Hydrolysis of this rigid gold complex **114** then provided the nitrogen containing five membered heterocycle **108**.



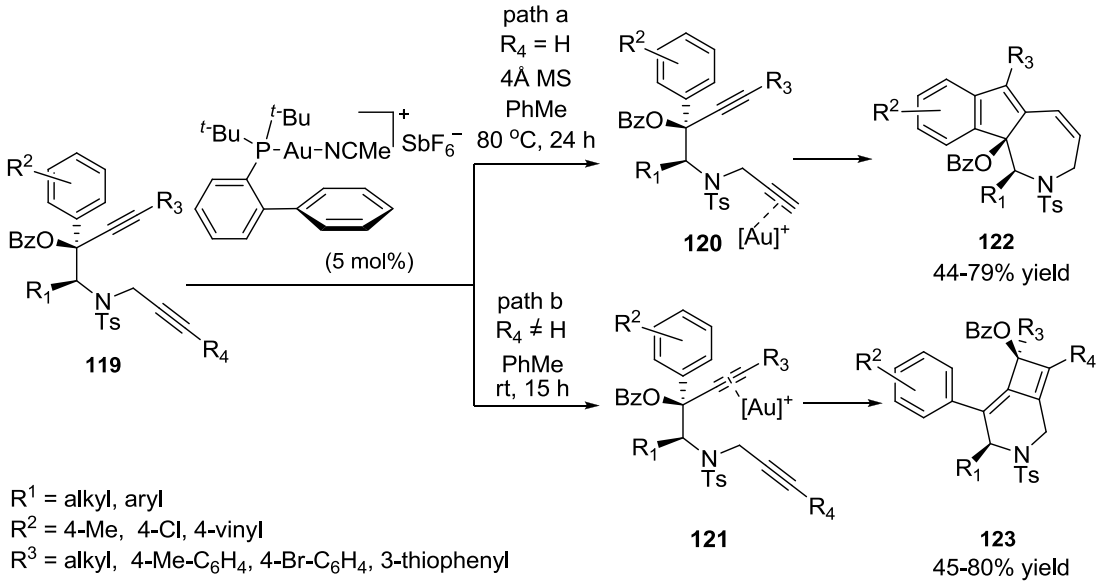
Scheme 1.27 Gold(I) catalyzed cyclization of nitrogen containing 1,6-diyne esters

In the same year, Malacria and co-workers disclosed the cycloisomerization of 1,6-diyne esters **115** containing a terminal alkyne moiety to δ-diketones **116** via an unprecedented 1,5-acyl migration as shown in Scheme 1.28.[47] It was proposed that the gold(I) catalyst first selectively activated the alkyne next to the ester group to facilitate [3,3]-sigmatropic rearrangement of the ester group in the substrate to give allene intermediate **117**. The gold(I) catalyst was then reasoned to activate the pendant terminal alkyne unit, which triggered a 5-*exo-dig* cyclization to provide acylium ion species **118**. Further 1,5-acyl migration of the acylium ion subsequently furnished the δ-diketone **116** in moderate to high yields of 70-99%. The limitation of this seminal work is the substituent on the alkynes. If a disubstituted propargyl ester was used, the second triple bond must be monosubstituted, otherwise complex mixtures were obtained.



Scheme 1.28 Gold catalyzed cyclization of 1,6-diyne esters to δ-diketones

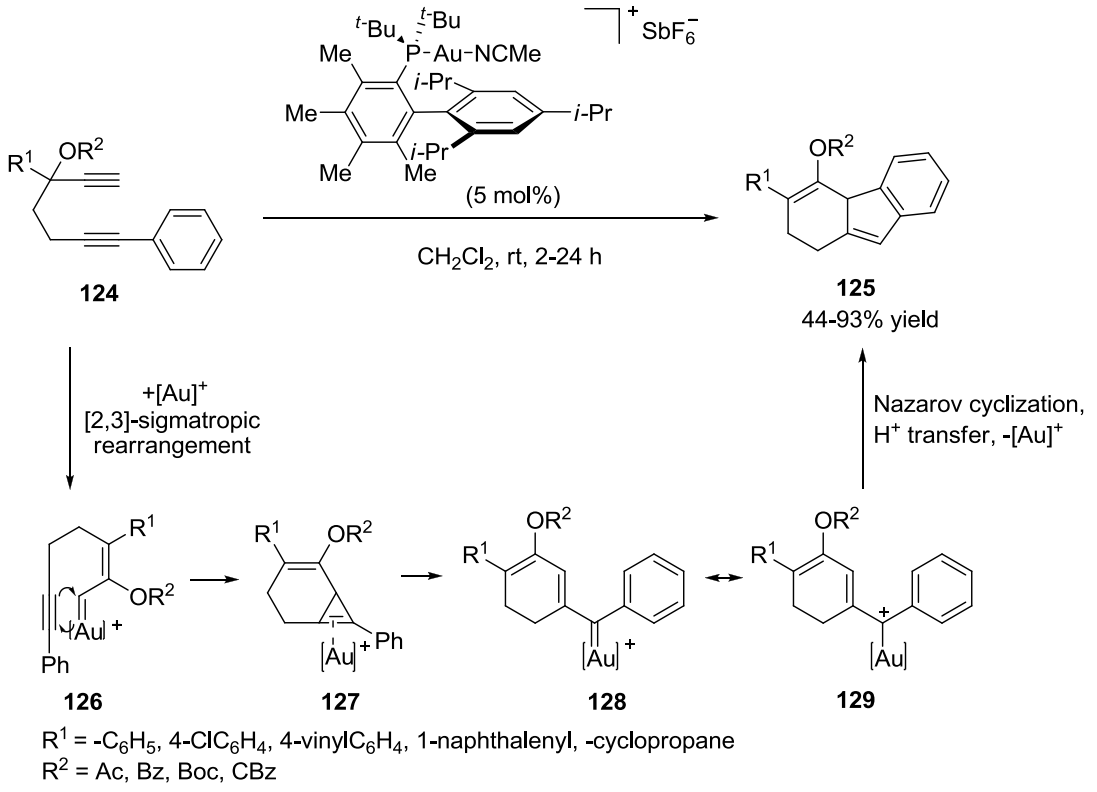
In 2012, Chan and co-workers reported the tandem gold(I) catalyzed cycloisomerization of 1,7-diyne benzoates **119** to give tricyclic product **122** in 44-79% yield and bicyclic product **123** in 45-80% yield (Scheme 1.29).[48] In this work, the substitution pattern of the tethered alkyne unit was shown to dictate the formation of the two different products. When a terminal alkyne was deployed, gold(I) complex catalyst was proposed to activate the less sterically hindered terminal alkyne to give the putative gold(I)-coordinated species **120**, as depicted in Scheme 1.29, path a. This newly formed species was then thought to undergo a concerted 5-*endo-dig* followed by a 7-*endo-dig* cyclization process which involved a nucleophilic attack by the aryl moiety to provide the tricyclic product **122**. On the other hand, when an internal alkyne was examined, it was proposed that the gold(I) complex catalyst would activate the triple bond next to the ester group to give the putative gold(I)-coordinated species **121**, as depicted in Scheme 1.29,



Scheme 1.29 Gold catalyzed cyclization of 1,6-diyne esters to δ-diketones

pathway b. An initial [3,3]-sigmatropic rearrangement of the benzoate moiety in the substrate followed by Prins-type cyclization would then give the bicyclic product **123**. It is worthy to take note that this work demonstrated the first example of selective activation in substrates containing two alkyne moieties in gold catalysis.

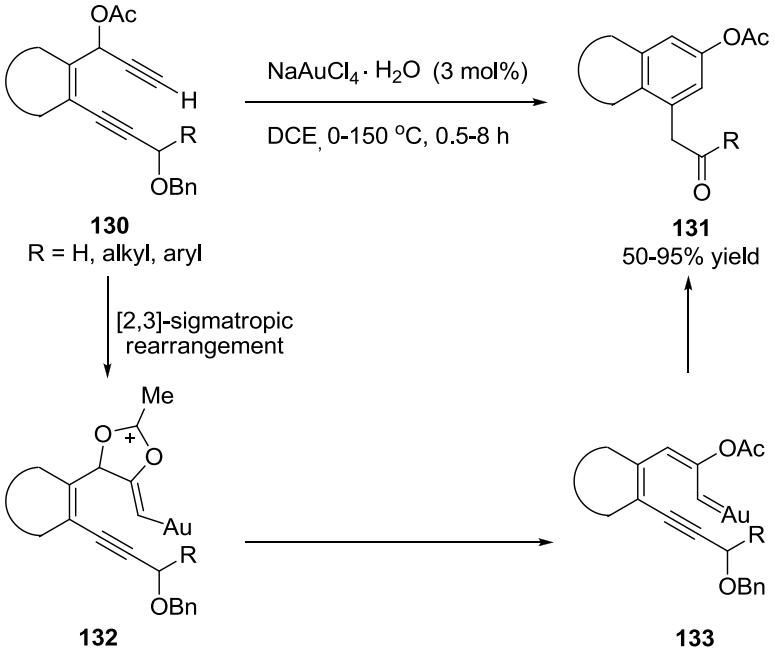
A year later, the same group reported another use of 1,*n*-diyne carbonates and esters in gold catalysis (Scheme 1.30).[49] In this work, 1,6-diyne esters **124** was found to furnish 2,4a-dihydro-1*H*-fluorenes **125** in 44-93% yields. It was proposed that an initial [2,3]-acyloxy migration of the ester group in the substrate occurred to form gold carbenoid species **126**. This newly formed adduct was thought to undergo cyclopropenation to give the cyclopropene intermediate **127**. Further activation of this



Scheme 1.30 Gold(I) catalyzed cyclisomerization of 1,6-diyne esters **124**

intermediate by gold(I) catalyst triggered the ring opening of the cyclopropene moiety to produce gold carbenoid **128**, which resonate to form a gold-stabilized allylic carbocation **129**. Nazarov cyclization followed by proton transfer and demetallation then took place to furnish 2,4a-dihydro-1*H*-fluorenes **125**. The proposed mechanism put forward in this work was confirmed via two-layer our own n-layered integrated molecular orbital and molecular mechanics (ONIOM (QM:QM')) computational studies using Gaussian 09.

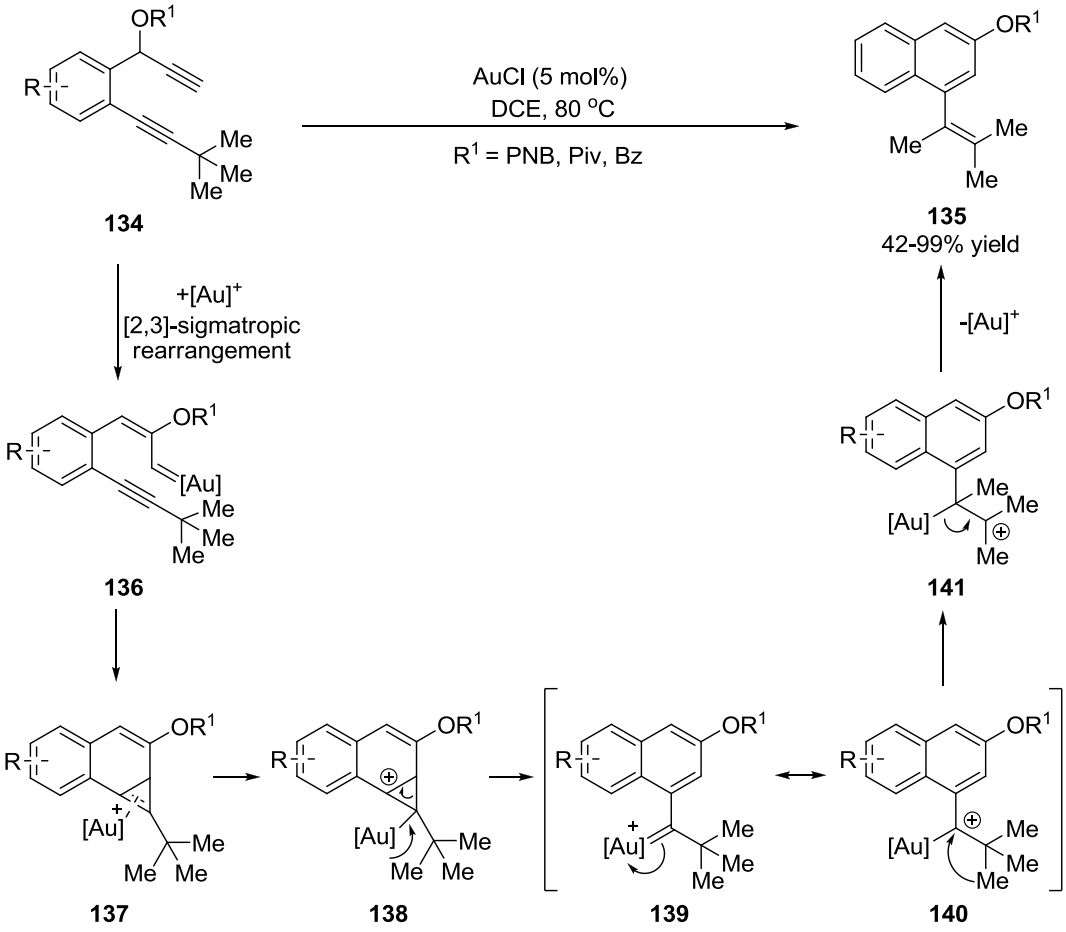
In the same year, Oh and co-workers reported the cycloisomerization of 1,6-diyne esters utilizing the selective activation concept put forward by our group (Scheme 1.31).[50] In this work, diyne esters **130** was reported to produce 2-acetoxynaphthalene derivatives **131** in moderate to high yields of 50-95% in the presence of a gold(III) catalyst. It was surmised that selective activation of the terminal alkyne triggered a [2,3]-sigmatropic



Scheme 1.31 Intramolecular ene-type reaction of gold carbenoid

rearrangement of the acetate group in the susbtrate via the five membered oxonium ring intermediate **132** to produce gold carbenoid **133**. This newly formed gold carbenoid **133** was then proposed to undergo an ene-type reaction to furnish 2-acetoxynaphthlene derivatives **131**.

At about the same time, Hashmi and co-workers reported the gold catalyzed cycloisomerisation reaction of 1,6-diyne carbonates and esters with a phenyl backbone **134** to vinyl-substituted b-naphthol derivative **135** (Scheme 1.32).[51] In this work, an initial [2,3]-sigmatropic rearrangement of the propargylic ester group in the 1,6-diyne

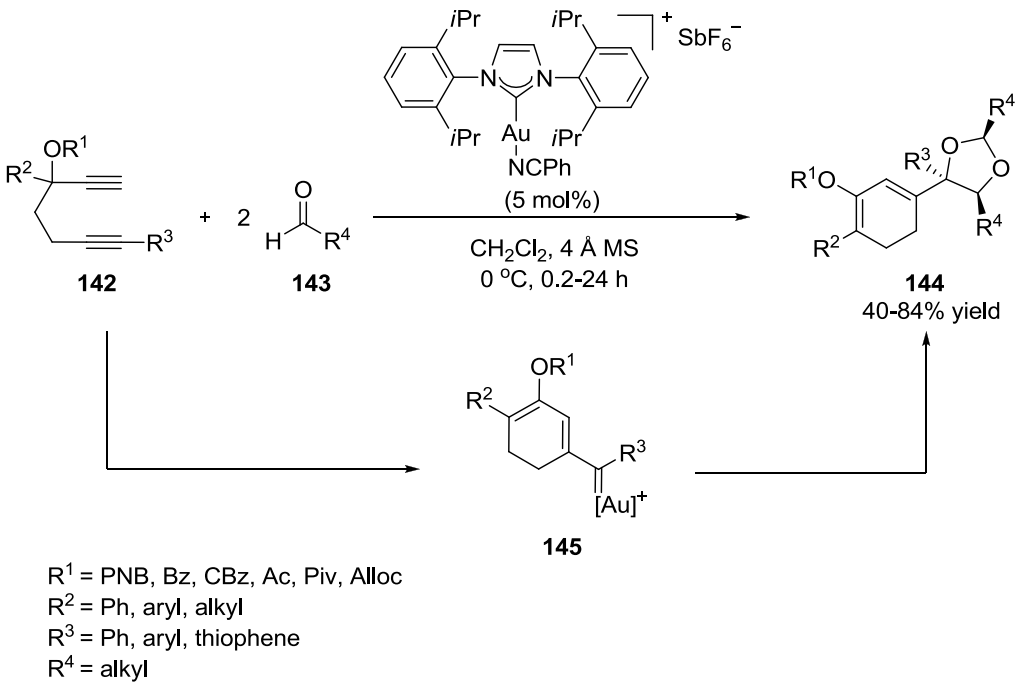


Scheme 1.32 1,7-carbene transfer in gold catalysis

esters **134** was proposed to generate gold carbenoid species **136**. A 1,7- transfer of the carbenoid moiety from gold carbenoid adduct **136** to that of **139** was thought to happen via trapping of gold carbenoid moiety of **136** by the pendant alkyne moiety to give the cyclopropene containing intermediate **137**. Activation of the alkene in the cyclopropene by the gold(I) catalyst induced ring opening via **138** to generate the benzyl stabilized carbenoid **139**. A final 1,2-shift of a methyl group to the carbocationic center of **140** occurred to give **141**. Protodeauration of this carbonium species then delivered the vinyl-substituted b-naphthol derivative **135** as the final product in a moderate to high yields of 42-99%.

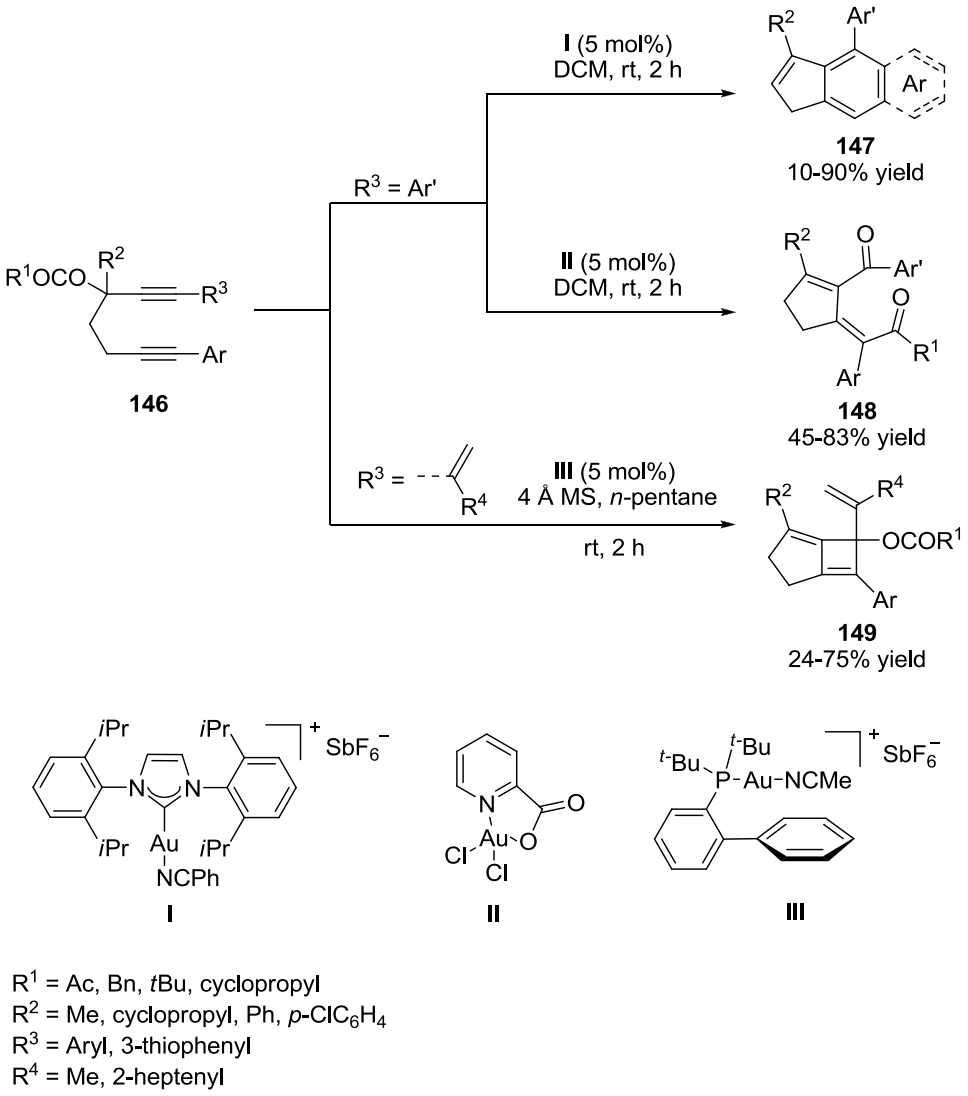
Recently, Chan and co-workers disclosed an unprecedented [2+2+1] cycloaddition reaction of 1,6-diyne carbonates and esters **142** with aldehydes **143** to furnish 4-(cyclohexa-1,3-dienyl)-1,3-dioxolane **144** in moderate to good yields of 40-84% (Scheme 1.33).[52] It was proposed that an initial [2,3]-sigmatropic rearrangement of the ester group in the substrate occurred. Subsequent cyclopropenation and ring opening could then provide the alkenyl gold carbenoid species **145**. This newly formed adduct was thought to undergo a [2+2+1] cycloaddition with two molecules of aldehylde **143** to give the 4-(cyclohexa-1,3-dienyl)-1,3-dioxolane product **144**.

In 2014, the same group delineated another gold catalyzed cycloisomerization of 1,6-diyne esters **146** to 1*H*-cyclopenta[*b*]naphthalenes **147**, *cis*-cyclopenten-2-yl *δ*-diketones **148** and bicyclo[3.2.0]hepta-1,5-dienes **149** (Scheme 1.34).[53] These three classes of products were obtained via three different pathways, depending on nature of gold(I) and gold(III) complex catalysts, substitution patterns in the substrates and reaction conditions. In the presence of NHC-gold complex **I** as the catalyst, substrates with a



Scheme 1.33 Gold catalyzed [2+2+1] cycloaddition of 1,6-diyne esters with aldehyde

pendant aryl group at the estereal alkynyl position (R^3 = Ar) were reasoned to undergo [3,3]-sigmatropic rearrangement followed by 5-*exo*-*dig* cyclization and Friedel-Crafts reaction to give 1*H*-cyclopenta[*b*]naphthalenes **147** in 10-90% yield. In contrast, the analogous reactions with gold(III) complex catalyst **II** were shown to afford *cis*-cyclopenten-2-yl *δ*-diketones **148** in 45-83% yield via preferential [3,3]-sigmatropic rearrangement followed by 5-*exo*-*dig* cyclization and 1,5-acyl migration. When the estereal alkynyl position was changed from an aryl to vinyl substituent (R^3 = vinyl) and gold(I) complex catalyst **III** was employed in the presence of 4 Å molecular sieves as drying agent, an initial [3,3]-sigmatropic rearrangement followed by 5-*exo*-*dig* cyclization was thought to take place. Subsequent Prins-type [2+2] cycloaddition was proposed to give bicyclo[3.2.0]hepta-1,5-dienes **149** in 24-75% yield.



Scheme 1.34 Gold catalyzed cycloisomerization of 1,6-enyne esters **146**

1.6 Proposed work

The work of this thesis has been directed toward providing efficient and novel synthetic strategies to access azaheterocycles, carbocycles and spirocycles from easily accessible 1,*n*-enyne and 1,*n*-diyne ester and carbonate as starting materials. In addition, these works have also been aimed at developing intramolecular based reactions that are atom economical and use low catalyst loadings along with operationally simple and mild

conditions to give complex cyclic compounds in one step. This was accomplished by exploiting the Lewis acidity of gold complexes towards unsaturated π-bonds in 1,*n*-enyne and 1,*n*-diyne esters and carbonates.

Thus, one of the goals of this project was to explore novel gold catalyzed methodologies utilizing 1,7-enyne esters for the construction of *cis*-1,2,3,6-tetrahydropyridin-4-yl ketone derivatives. It was envisioned that by harnessing the difference in the rate of protodeauration between various gold(I) complexes, divergent mechanistic pathways could provide a variety of product scaffolds chemoselectively. Generally, the rate of protodeauration of the NHC-gold(I) complexes is slower than that of gold(I)-phosphine complexes.[54] Owing to this, we anticipated that NHC-gold(I) complexes would lead to 1,5-acyl migration affording δ-diketone substituted 1,2,3,6-tetrahydropyridine adducts. On the other hand, reactions catalyzed by gold(I)-phosphine complexes were envisaged to undergo faster protodeauration to produce *cis*-1,2,3,6-tetrahydropyridin-4-yl ketone derivatives.

The second focus of this project has been to assess the effect of exchanging the alkene moiety at a1,*n*-enyne substrates to a diene moiety in 1,*n*,*m*-dienyne starting materials. In order to do this, 1,6,8-dienyne carbonates and esters were designed and envisioned to form *cis*-cyclohepta-4,8-diene-fused pyrrolidines via a cascade reaction involving an equilibrium between [2,3]- and [3,3]-sigmatropic rearrangement of the ester group in the substrate.

In the final section of this work, we surmised that 1,*n*-diyne esters and carbonates bearing a pendant alkene moiety may feasibly undergo synthetically interesting transformations in the presence of gold(I) catalysts. In such, 1-ene-4,10-diyne esters were

designed and reasoned to undergo an initial gold-activated metallo-Nazarov type cyclization followed cycloisomerizations involving the pendant alkyne moiety to provide a wide variety of spiro[4.5]decen-1-one and spiro[4.4]nonen-1-one derivatives.

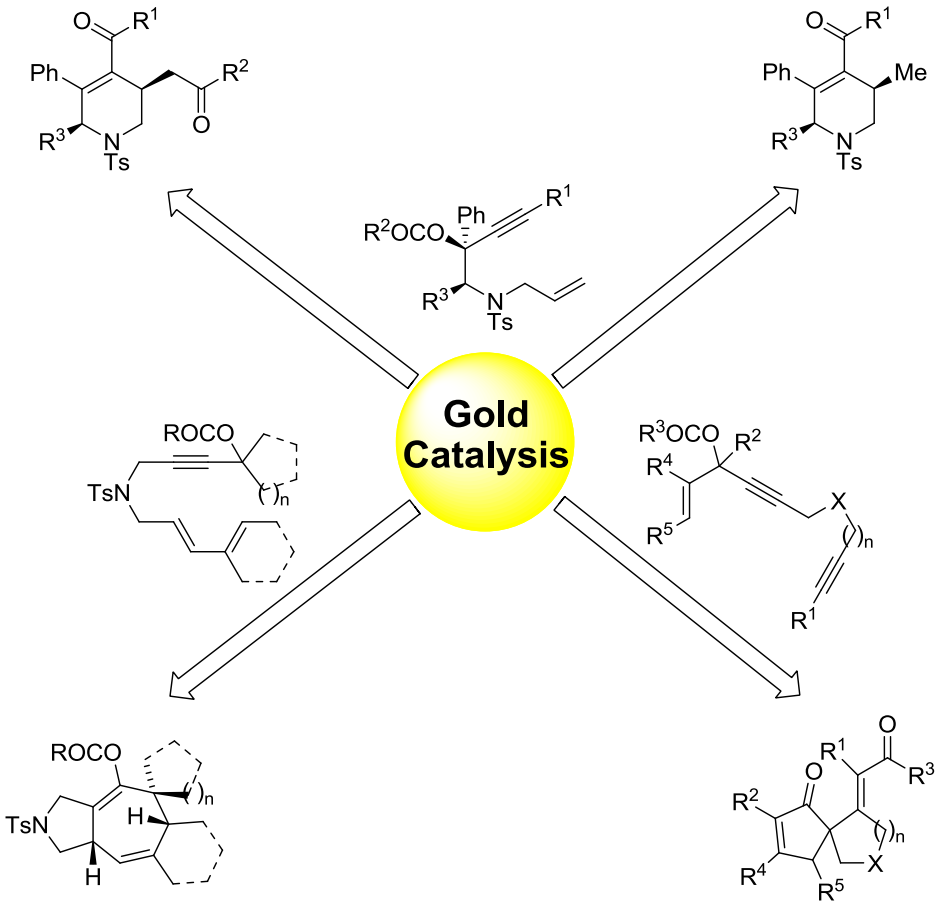


Figure 1.2 Gold catalyzed synthesis of cyclic compounds from 1,*n*-enyne and 1,*n*-diyne esters and carbonate

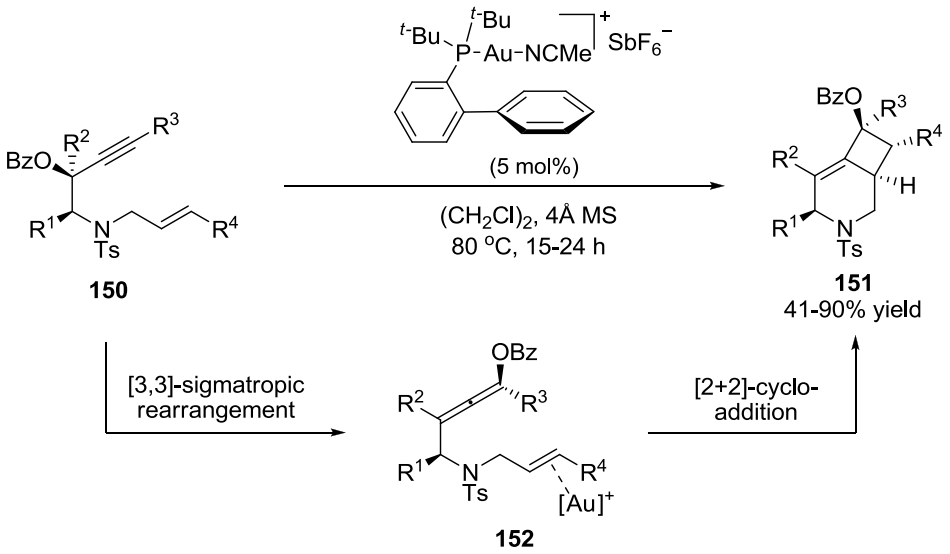
Chapter II. Gold Catalyzed Cycloisomerization of 1,7-Enyne Esters to Structurally Diverse *cis*-1,2,3,6-Tetrahydropyridin-4-yl Ketone

2.1 Introduction

Further functional group transformations of the Au(I)-carbenoid adduct or 1,*n*-allenene intermediate, which are formed from the [2,3]- or [3,3]-sigmatropic rearrangement of the propargyl ester moiety in 1,*n*-enyne carbonates and esters mediated by gold(I) catalysts (Chapter I, Section 1.3), have remained desirable despite the progresses made in this field since the early 21st century. Methods for the functionalization of the Au(I)-carbenoid adduct are often based on its carbenoid reactivity,[55] whilst transformations of the 1,*n*-allenene are generally carried out via the activation of the allene moiety by the metal catalyst.[56] In contrast, strategies based on the selective activation of the alkene moiety instead of the allene moiety of the 1,*n*-allenene intermediate by the gold(I) complex catalyst have been less widely explored.

The first and only work for this novel mode of activation prior to this study was reported by our group in 2011 (Scheme 2.1).[57] In this work, 1,7-enyne benzoates **150** was reported to undergo a tandem [3,3]-migration/[2+2] cycloaddition to afford azabicyclo[4.2.0]oct-5-enes **151** in 41-90% yield in the presence of a gold(I) catalyst. The activation of one of the two unsaturated systems in the allenene intermediate **152** was thought to be purely based on the difference in steric hindrance. The presence of substituents on the allene moiety was reasoned to hinder the gold(I) complex catalyst from activating it, resulting in the selective activation of the less sterically hindered

alkene moiety instead. Furthermore, it is noteworthy that this work served as evidence supporting the viability of gold-catalyzed cycloisomerization processes involving the alkene moiety in 1,*n*-enynes scaffold which was previously reported to be resistant in the acyloxy substituted 1,6-enynes generated from dipropargylic amides.[58]



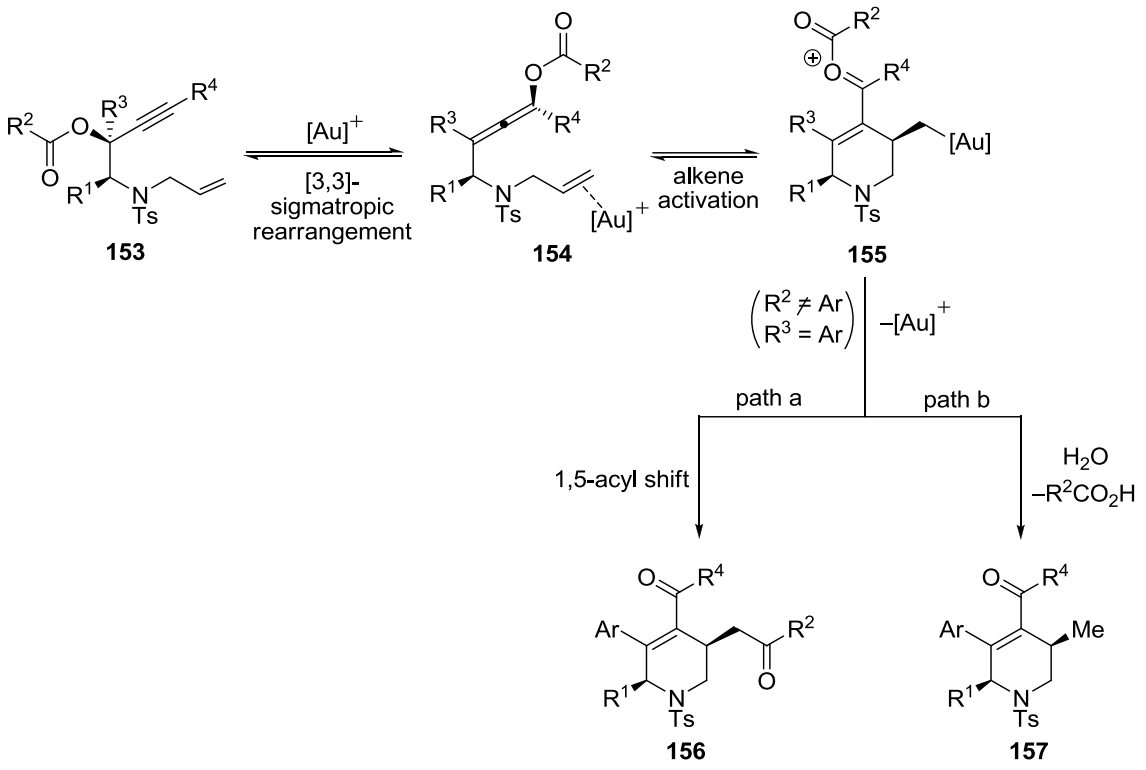
Scheme 2.1 Gold-catalyzed tandem [3,3]-migration/[2+2] cycloaddition of 1,7-enyne benzoates **150** via a selective activation of alkene moiety in the allenene intermediate

Inspired by the mechanistic premise put forward, we reasoned that another type of transformation pathway utilizing a similar 1,7-enyne esters to provide access to other members of the piperidine family of compounds could be achieved by control of the electronic and steric interactions between the substituents in the substrate and the ligands in gold catalyst. To our delight, we discovered that when R^2 is not an Ar group and R^3 is an Ar group in 1,7-enyne ester **153** was subjected to NHC-gold(I) complex catalyst,

the resulting organogold species **155** formed *in situ* from the selective activation of the alkene moiety in the allenene intermediate **154** was susceptible to 1,5-acyl migration process giving the *N*-heterocycles adduct, *cis*-1,2,3,6-tetrahydropyridin-4-yl δ-diketone **156** (Scheme 2.2, path a). This form of reactivity represents an unprecedented construction of a C–C bond via 1,5-acyl migrations to a Au–C(sp^3) moiety of an alkyl gold species. The only other known example of a 1,*n*-acyl migration to a Au–C(sp^3) moiety prior to this work is a 1,3-acyl migration, which was suggested in gold(I) catalyzed transformation of propiolic acids to 4-hydroxy-α-pyrones.[59] This contrasts to the emergence of gold-catalyzed methods for C–C bond formation involving 1,5-acyl migration of a vinyl gold intermediate.[47] On the other hand, the use of a gold(I)-phosphine complex catalyst was shown to cause the substrate to undergo the similar [3,3]-sigmatropic rearrangement/6-*exo*-*trig* cyclization to organogold species **155**, followed by a more rapid hydrolysis pathway, owing to the faster rate of protodeauration of gold(I)-phospine complexes (Chapter I, section 1.6), delivering *cis*-1,2,3,6-tetrahydropyridin-4-yl ketone derivatives **157** as depicted in Scheme 2.2, path b.

As a part of ongoing studies in our group in the synthesis of cyclic compounds via Lewis acidic gold catalysis,[60] we describe herein the details of this chemical transformation that offers a convenient and chemically selective route to these two *N*-heterocyclic products in high yields. The *cis*-1,2,3,6-tetrahydropyridine products, a valuable structural motif in various of biologically active natural products, were obtained as single regio-, diastereo- and enantiomers, with the latter showing efficient chirality transfer from the substrate to the product during the nitrogen ring-formation process.

Additionally, we present herein the application of this methodology to synthesize an enantiopure analogue of the 2,3,4,4*a*,5,9*b*-hexahydroindeno[1,2-*c*]pyridines, which are known to exhibit antispermatogenic, antidepressant and antiintegrin activity.[61]

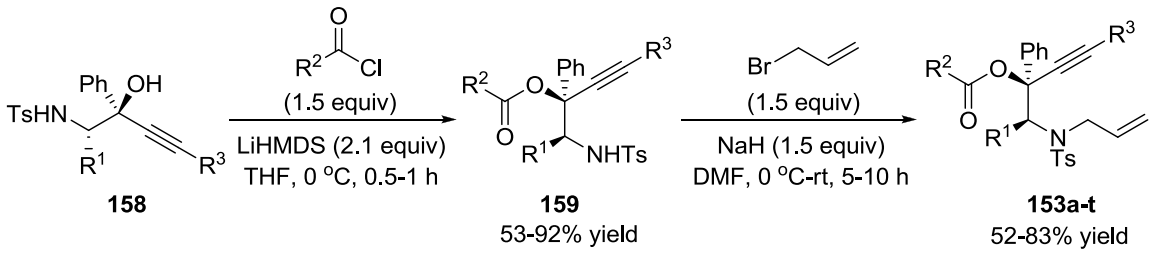


Scheme 2.2 Product divergence in gold-catalyzed cycloisomerization of 1,7-enyne ester

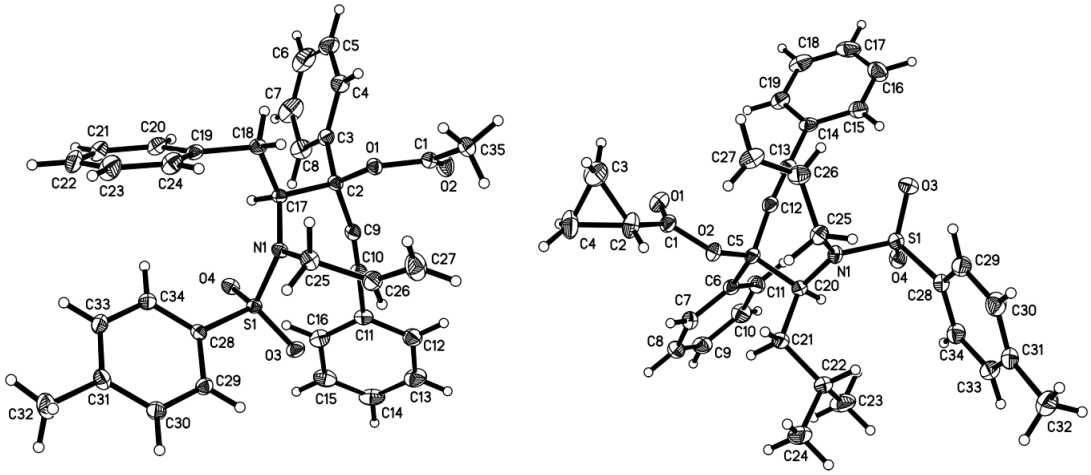
2.2 Results and Discussion

The 1,7-enyne esters utilized in this work were prepared from the *N*-allyl-*N*-((3*S*,4*S*)-3-hydroxy-1,3,5-substituted-alk-4-yn-2-yl)-4-methylbenzenesulfonamide **158**, with the latter being synthesized from various L-α-amino acid following literature procedures (Scheme 2.3).[48,57] With this in hand, the alcohol **158** was protected with several non-

aromatic protecting groups by utilizing LiHMDS as base in THF with appropriate acyl chlorides to give the intermediates **159** in 53-92% yields. This was followed by allylic alkylation of the amine unit with NaH as a base in DMF and allyl bromide to give the 1,7-enyne esters **153** in 52-82% yield. X-ray crystallographic analysis of the substrates was done to determine the (3*S*,4*S*) absolute configuration of the 1,7-enyne esters **153a** and **153n** (Figure 2.1).[62]



Scheme 2.3 Synthesis of 1,7-enyne esters **153**



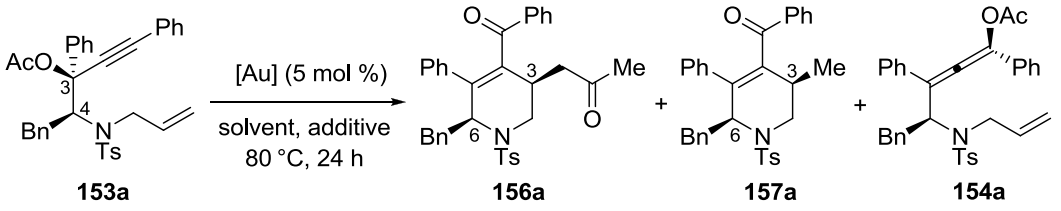
(a) **153a** (b)**153n**

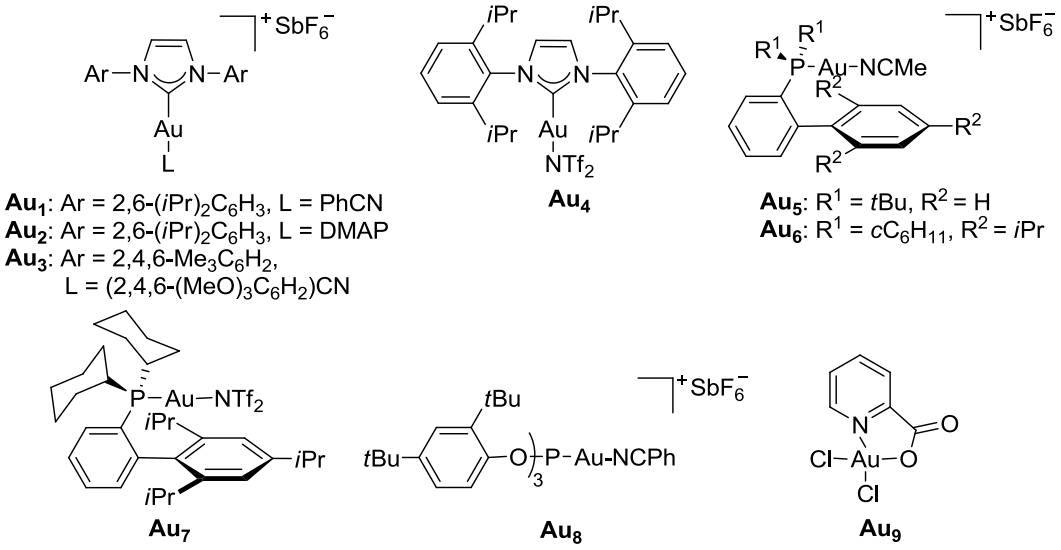
Figure 2.1 ORTEP drawings of **153a** (a) and **153n** (b) with thermal ellipsoids at 50% probability levels

Next, we sought to establish the optimum reaction conditions by employing an enantiopure *syn*-1,7-enyne acetate **153a** which was successfully synthesized from L-phenylalanine as a model substrate (Table 1). Initial study revealed that in the presence of 5 mol% of NHC-gold(I) catalyst $\mathbf{Au_1}$ in 1,2-dichloroethane (DCE) at 80 °C for 24 h, *syn*-1,7-enyne acetate **153a** was found to give **156a** in 60% yield and **157a** in 16% yield, and in both cases, as a single regio-, diastereo- and enantiomer (entry 1). The *cis* stereochemistry as well as the absolute configuration of the two azaheterocyclic products were ascertained via X-ray crystallographic analysis (Figure 2.2).[62] Subsequently, adding 4 Å molecular sieves (MS) as a drying agent led to **156a** being obtained in the same product yield with no formation of **157a** observed and 1,6-allene **154a** furnished in 12% yield (entry 2). It is noteworthy that the formation of 1,*n*-allene in gold catalysis has been well documented.[63] Moving on, in order to suppress the formation of the 1,6-allenene **154a**, catalyst loading was increased from 5 to 10 mol%, which to our delight furnished only the δ-diketone **156a** in 75% yield (entry 3). Changing the solvent from 1,2-dichloroethane to other solvents such as toluene, acetonitrile or tetrahydrofuran in the presence of 10 mol % of gold-phosphine catalyst $\mathbf{Au_1}$ was found to be ineffective, resulted in low or no formation of any of the azaheterocyclic products, giving only the 1,6-allenene **154a** in low to good yields of 35-81% (entries 4-6). An exception was observed when PhMe was used as the solvent, which afforded the ketone **157a** in 35% yield in addition to the aforementioned **154a** (entry 4). With the best solvent on hand, a screening of different Au(I) and Au(III) complexes as catalysts which were prepared following literature procedures was carried out (entries 7-18).[64] In general, subjecting

153a to 5 mol% of other gold(I) and gold(III) complexes as catalyst were found to be markedly less effective. 1,6-allenene **154a** was obtained as the only product in high yields of 81 and 86% when the reaction was carried out in the presence of NHC-gold(I) complexes **Au$_2$** and **Au$_3$**, respectively (entries 7-8). Deploying AuCl and Au(III) complex **Au$_9$** as catalysts were also found to be ineffective, giving **154a** in respective yields of 67 and 85% (entries 17-18). All three adducts were obtained in low yields of 28, 11 and 23% when the reaction was carried out with NHC-gold(I) complex **Au$_4$** as the catalyst (entry 9). Similarly, replacing **Au$_1$** with gold(I) phosphine complex catalysts **Au$_5$**-**Au$_7$** and $Ph_3PAuNTf_2$ resulted in a mixture of **156a** and **157a** being obtained (entries 10 and 13-15), whereby employing Au(I) phosphite **Au$_8$** as catalyst was found to give a mixture of **157a** and **154a** (entry 16). As shown in entry 10, gold(I) phosphine catalyst **Au$_5$** demonstrated a potential of furnishing ketone **157a** as a sole product. This was further inspected by subjecting **153a** with **Au$_5$** in the absence of 4 Å MS, in which allowed the formation of **157a** in 84% yield (entry 11). An increase in the yield of the ketone product **157a** to 96% was further observed when 2 equiv of water was added as a proton source into the reaction (entry 12). With these results on hand, two optimized reaction conditions were obtained. The reaction of 1,7-enyne ester **153a** with 10 mol% of NHC-gold(I) catalyst **Au$_1$** and 4 Å MS as a drying agent in DCE as a solvent at 80 °C for 24 h afforded the best conditions to obtain *δ*-diketone substituted *cis*-1,2,3,6-tetrahydropyridine derivative **156a** while reaction of **153a** in the presence of 5 mol% of gold(I) phosphine complex **Au$_5$** with an addition of 2 equiv of water in DCE at 80 °C for 24 h provided the optimum conditions to the formation of *cis*-1,2,3,6-tetrahydropyridin-4-yl ketone product **157a**.

Table 2.1 Optimization of the reaction conditions[a]



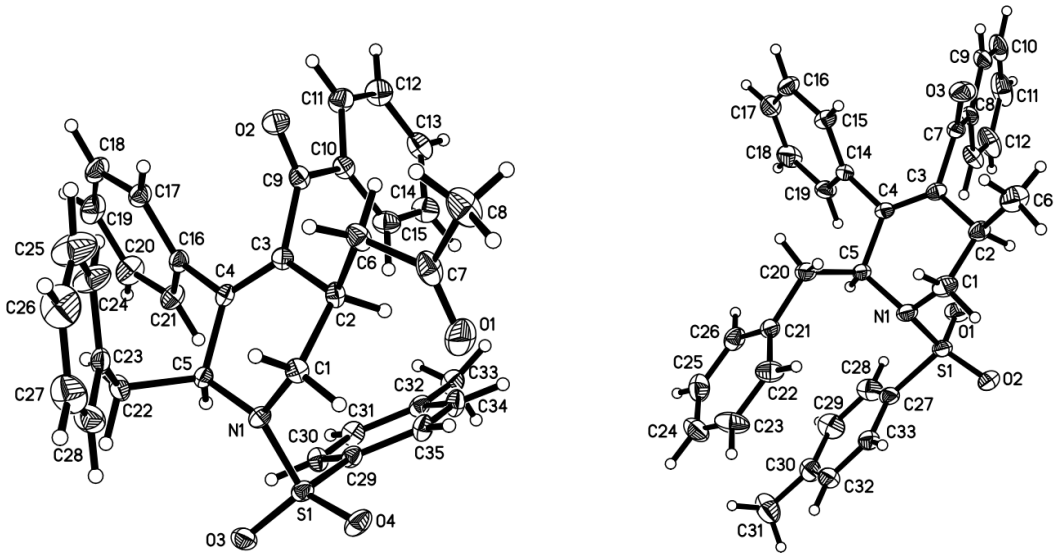


Entry	Catalyst	Solvent	Yield (%)[b]		
			156a	**157a**	**154a**
1[c]	**Au$_1$**	$(CH_2Cl)_2$	60	16	-
2	**Au$_1$**	$(CH_2Cl)_2$	60	-	12
3[d]	**Au$_1$**	$(CH_2Cl)_2$	75	-	-
4[d]	**Au$_1$**	PhMe	-	23	35
5[d]	**Au$_1$**	MeCN	-	-	67
6[d]	**Au$_1$**	THF	-	-	81
7	**Au$_2$**	$(CH_2Cl)_2$	-	-	86

Table 2.1 *(continued).*

Entry	Catalyst	Solvent	Yield (%)[b]		
			156a	**157a**	**154a**
8	**Au$_3$**	$(CH_2Cl)_2$	-	-	81
9	**Au$_4$**	$(CH_2Cl)_2$	28	11	23
10	**Au$_5$**	$(CH_2Cl)_2$	14	69	-
11[c]	**Au$_5$**	$(CH_2Cl)_2$	-	84	-
12[c,e]	**Au$_5$**	$(CH_2Cl)_2$	-	96	-
13	**Au$_6$**	$(CH_2Cl)_2$	12	71	-
14	**Au$_7$**	$(CH_2Cl)_2$	31	48	-
15	$Ph_3PAuNTf_2$	$(CH_2Cl)_2$	10	70	-
16	**Au$_8$**	$(CH_2Cl)_2$	-	53	15
17	AuCl	$(CH_2Cl)_2$	-	-	67
18	**Au$_9$**	$(CH_2Cl)_2$	-	-	85

[a] All reactions were carried out at the scale of 0.2 mmol with catalyst:**153a** ratio of 1:20 and 100mg of 4Å MS at 80 °C for 24 h. [b] Isolated yield. [c] Reaction carried out in the absence of 4Å MS. [d] Reaction carried out with 10 mol% of catalyst. [e] Reaction took place with an addition of 2 equiv of H_2O.



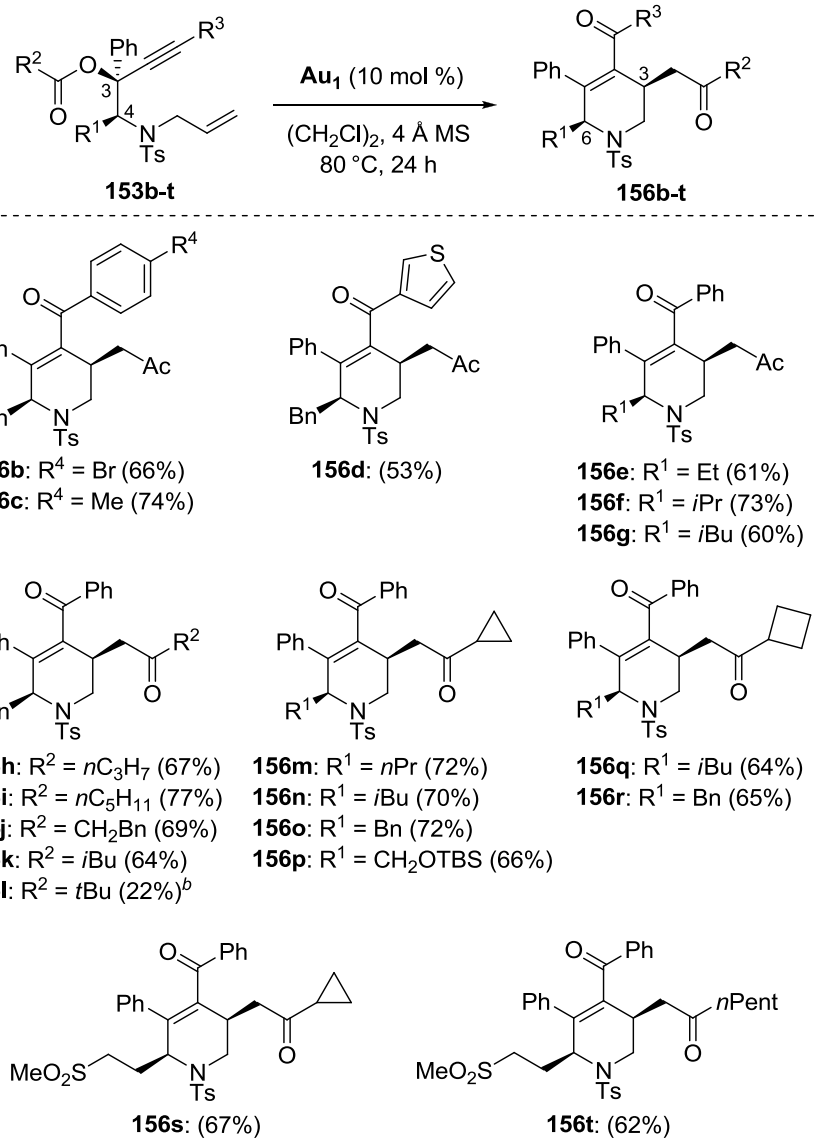
(a) **156a** (b) **157a**

Figure 2.2 ORTEP drawings of **156a** (a) and **157a** (b) with thermal ellipsoids at 50% probability levels

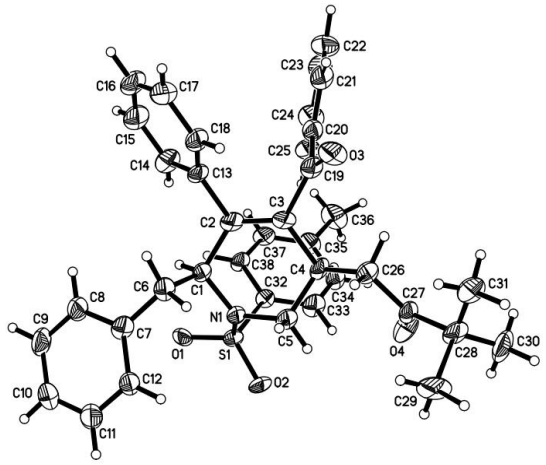
With two optimal conditions in hand, we first sought to evaluate the scope of the formation of the δ-diketone substituted *cis*-1,2,3,6-tetrahydropyridines **156b-t** for a series of 1,7-enyne carbonates and esters **153b-t** as depicted in Table 2.2. It was revealed that with 10 mol% of the NHC-gold(I) complex $\mathbf{Au_1}$ as the catalyst, the transformations was able to tolerate a large arrays of δ-diketone substituted *cis*-1,2,3,6-tetrahydropyridines in 22-77% yield. Starting materials containing an electron-withdrawing or electron donating group at the para position of the aryl substituent on the alkynyl carbon center such as **153b** and **153c** were found to furnish the corresponding diketone adducts **156b** and **156c** in moderate yields of 66 and 74%, respectively. The reaction conditions were also found

to be able to tolerate starting materials bearing a thiophene moiety at the C3 position (**153d**) or other linear alkyls (**153e**) and branched chain (**153f**,**g**) alkyl units at the amino carbon center. In these reactions, the corresponding δ-diketones *N*-heterocyclic products were funished in moderate to good yields of 53-73%. Further assessment on the scope of the methodology revealed that the alkyl or cycloalkyl units on the esters moiety **153h-k** and **153m-t** have no influence on the reaction, giving δ-diketones **156h-k** and **156m-t** in good yields of 64-77%. It is noteworthy that 1,7-enyne esters bearing a pendant heteroatom group such as OTBS (**153p**) or MeO_2S (**153s**,**t**) moiety produced the corresponding δ-diketones **156p** in 66% yield and **156s**,**t** in 62 and 67% yields, respectively. The only anomaly observed was that substrate containing a sterically bulky pivalate moiety (**153l**) required a higher catalyst loading of 20 mol% and a longer reaction time of 48 h to produce δ-diketone **156l** in 22% yield along with ketone **157a** in the 45% yield, respectively. More markedly, no detection of any bicyclic compounds arising from the possible Au(I)-mediated [2+2] cycloaddition pathway in the ^{1}H NMR analysis of the crude mixtures. This is in contrast to our earlier findings for the analogous reactions of 1,7-enyne benzoates[57] and those that has been widely reported of 1,6-allenenes.[65] This also suggested that highly selective nitrogen ring forming process was demonstrated in all of the cycloisomerization transformations. In addition, the δ-diketone azahetecyclic adducts were obtained as a single diastero- and enantiomer. With the aid of X-ray crystallographic analysis, the cis stereochemistry and (3*R*,6S) absolute configurations for **156l**, **156p**, and **156q** was further confirmed.[66]

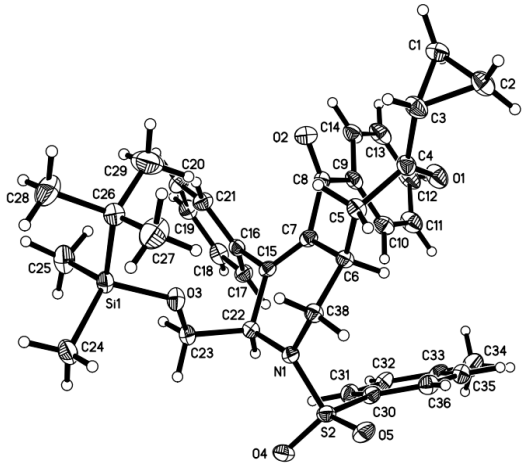
Table 2.2 Cycloisomerization of 1,7-enyne esters **153b-t** catalyzed by **Au_1**[a]



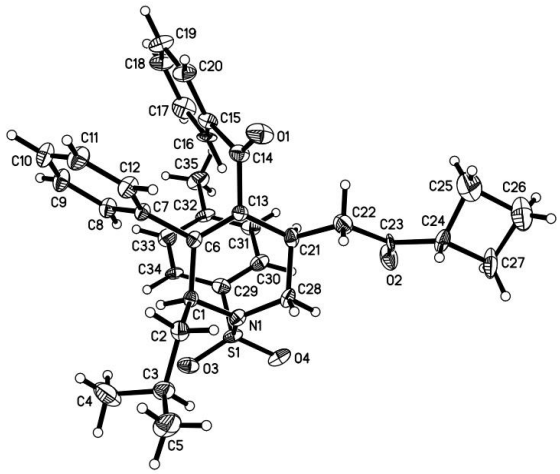
[a] Unless otherwise stated, all reactions were carried out at the 0.2 mmol scale with **Au_1**:**153** ratio = 1:10 and 4 Å MS (100 mg) in DCE at 80 °C for 24 h. Values in parentheses denote isolated product yields. [b] Reaction performed with 20 mol % of **Au_1** for 48 h and **157a** was obtained in 45% yield.



(a) **156l**



(b) **156p**

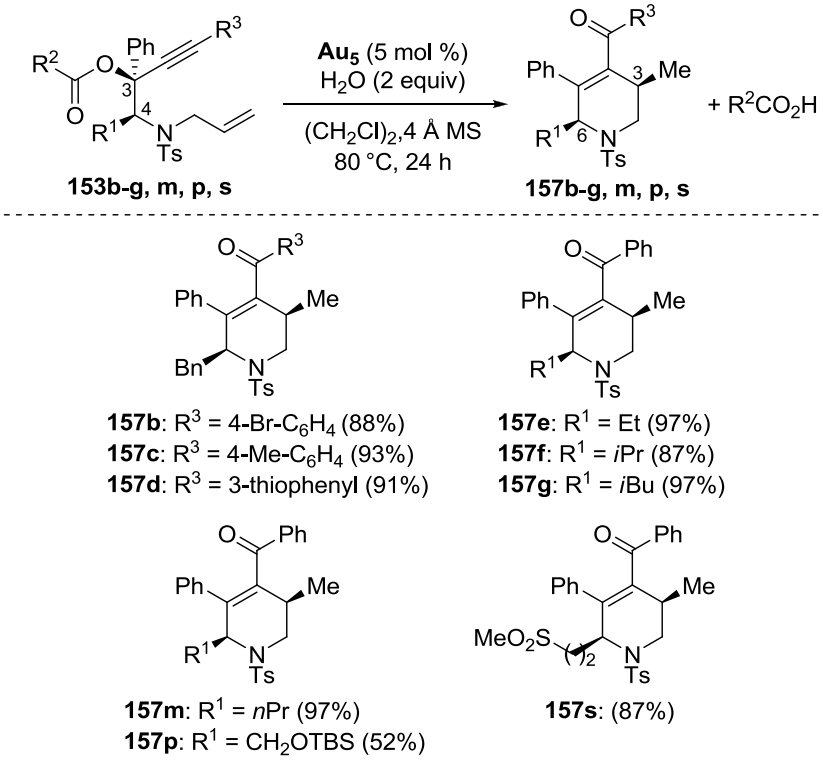


(c) **156q**

Figure 2.2 ORTEP drawings of **156l** (a), **156p** (b), and **156q** (c) with thermal ellipsoids at 50% probability levels

Next, we sought to define the generality of the cycloisomerization reaction which include hydrolysis instead of the 1,5-acyl migration in the last step. 1,7-enyne ester compounds **153b-g**,**m**,**p**,**s** were chosen as examples to give ketone **157b-g**,**m**,**p**,**s** derivatives (Table 2.3). On the whole, the transformations in the presence of 5 mol% of gold(I) phosphine complex $\mathbf{Au_5}$ as catalyst in 1,2-dichloroethane with 2 equiv of water were found to proceed well. Under this optimized conditions, the *cis*-1,2,3,6-

Table 2.3 Cycloisomerization of 1,7-enyne esters **153b-g**,**m**,**p**,**s** catalyzed by $\mathbf{Au_5}$[a]

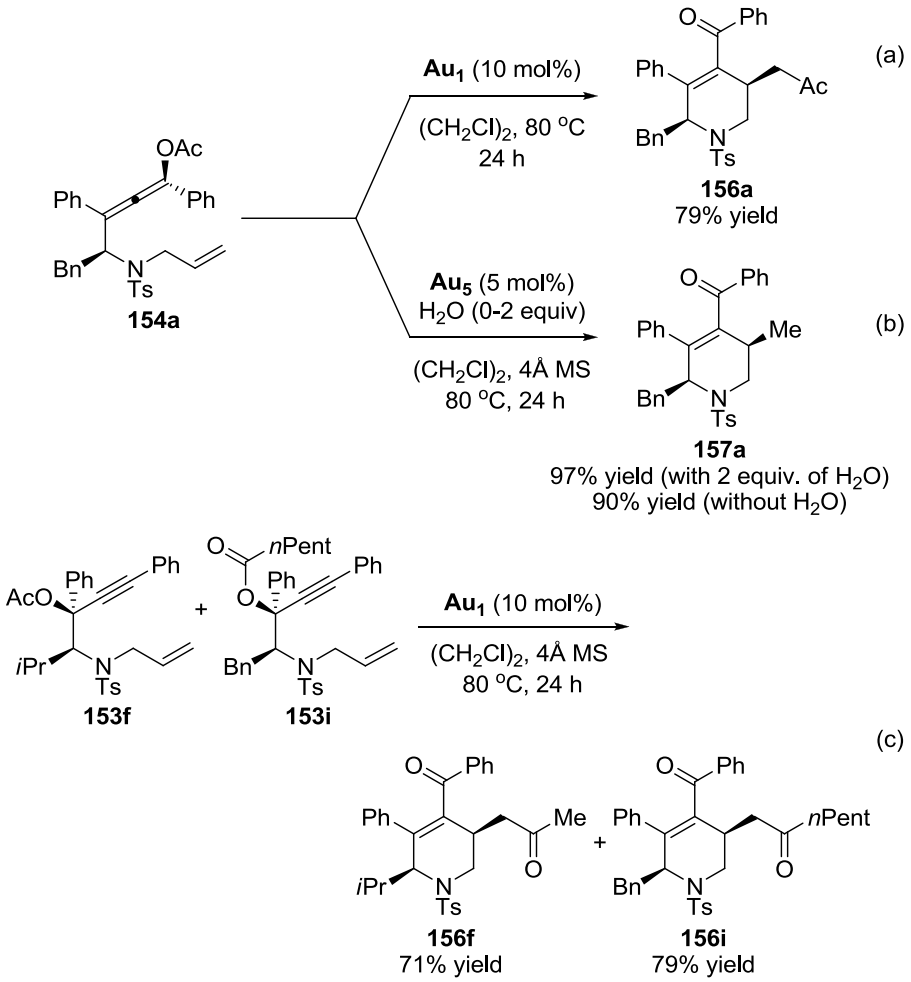


[a] All reactions were performed on 0.2 mmol scale with $\mathbf{Au_5}$:**153** ratio = 1:20 and 2 equiv of water in DCE at 80 °C for 24 h. Values in parentheses denote isolated product yields.

tetrahydropyridin-4-yl ketones **157b-g**,**m**,**p**,**s** were furnished in moderate to excellent yields of 52-97%, and as a single diastereo- and enantiomer on the basis of ^{1}H NMR measurements. It is noteworthy that the reactions of **153n** and **153q** under the same reaction conditions with Au(I) phosphine complex **Au$_5$** as the catalyst could also afford **157g** in excellent yields of 94 and 96%, respectively. Likewise, ketone adduct **157s** was able to be obtained in 83% yield by subjecting 1,7-enyne ester **153t** to Au(I) phosphine **Au$_5$** under these same conditions.

Based on the earlier work in our group[57] and the mechanistic ground depicted in Scheme 2.2, it was predicted that a common 1,6-allenene intermediate was involved in the Au(I)-catalyzed formation of the azaheterocyclic adducts. As depicted earlier in Table 2.1, the formation of **154a** for the reaction of **153a** under some circumstances suggested its participation in the Au(I)-catalyzed cycloisomerization route. This hypothesis was confirmed by several control reactions utilizing 1,6-allenene **154a**, as depicted in Scheme 2.4, a and b. When 1,6-allenene **154a** in DCE was treated with 10 mol% of **Au$_1$**, the expected δ-diketone adduct **156a** was obtained as the only product in a good yield of 79% (Scheme 2.4, eq a). Similarly, subjecting 1,6-allenene **154a** in 1,2-dichloroethane with 5 mol% of **Au$_5$** in place of **Au$_1$** in the absence of H_2O gave **157a** in 90% yield whilst repeating the reaction in the presence of 2 equiv of H_2O furnished **157a** in an excellent yield of 97% (Scheme 2.4, eq b). The role of the Au(I) complex as a Lewis acidic catalyst in selective activation of the alkene unit of the 1,6-allenene intermediate is also supported by our observations when a control reaction was carried out in the absence of catalyst. In this experiment, no reaction was observed and the

1,6-allene **154a** was recovered quantitatively. This result further confirmed that the cyclization of 1,6-allenenes bearing an unactivated alkene moiety **154** is not a thermally driven process, similar to what was reported in previous studies.[57,67] The involvement of an intramolecular 1,5-acyl shift in the cycloisomerization reactions with NHC-gold(I) catalyst **Au$_1$** was also corroborated by our findings, when a 1:1 mixture of **153f** an **153i**



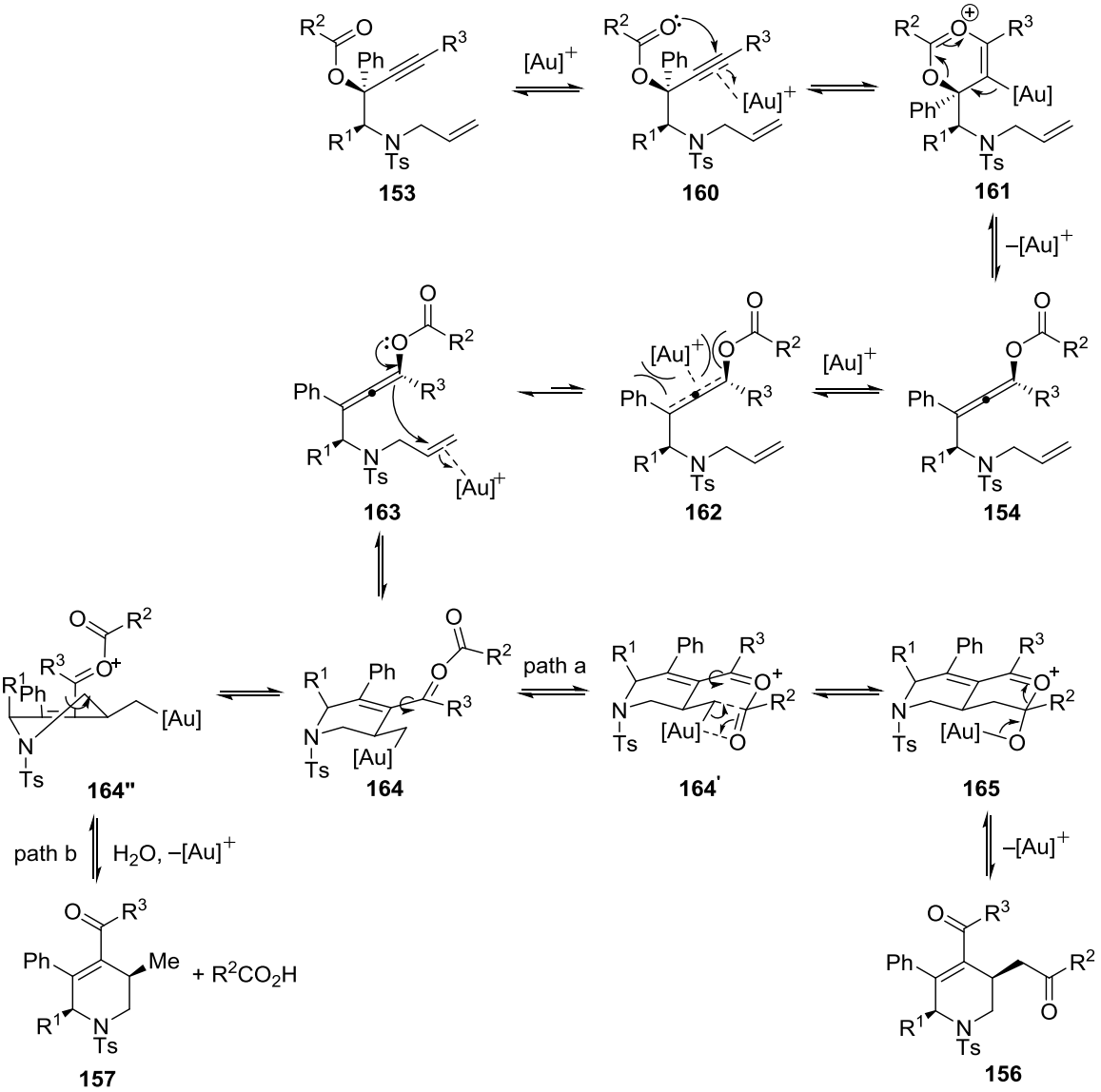
Scheme 2.4 Control experiments with **154a**, **153f** and **153i** catalyzed by Au(I) complex catalysts **Au$_1$** or **Au$_5$**

in 1,2-dichloroethane was subjected to the gold(I) complex **Au$_1$** under the optimized conditions, the formation of the corresponding δ-diketones **156f** in 71% yield and **156i** in 79% yield were obtained as the sole products, with no other types of δ-diketone or ketone obtained based on ^{1}H NMR analysis of the crude reaction mixture, as depicted in Scheme 2.4, eq c.

A plausible mechanism for this gold(I)-catalyzed cycloisomerization of **153** to form the *cis*-1,2,3,6-tetrahydropyridin-4-yl compounds is depicted in Scheme 2.5. In a mode similar to the earlier work reported by our group,[57] the alkyne unit was selectively activated over the alkene moiety in the 1,7-enyne ester **153** by the gold(I) complex was initially involved to furnish the gold-coordinated complex **160**. This results in a [3,3]-sigmatropic rearrangement of the carboxylate functionality in *syn* manner via the 1,3-dioxin-1-ium intermediate **161** to give 1,6-allenene **154**. Another selective coordination of the pendant alkene moiety over the allene moiety by the Lewis acidic gold(I) complex catalyst then took place to afford the gold-activated adduct **163** over that of **162**. This might have occurred due to unfavourable steric interactions between the gold(I) complex and the substituents on the allene moiety in the intermediate. Subsequently, the alkyl gold adduct **164** was afforded via an 6-*exo*-*trig* cyclization involving *anti* addition through the more nucleophilic distal 2π component of the allenic moiety to the Au(I)-activated alkene bond. It is noteworthy that this type of putative alkyl gold species have been proposed in several works.[68] Depending on the nature of the gold(I) complex employed, two different reactivity modes are thought to take place at this section in the proposed mechanism. The oxocarbenium complex **164** derived from the reactions of **153** catalyzed by **Au$_1$** could be more resistant to hydrolysis process as it

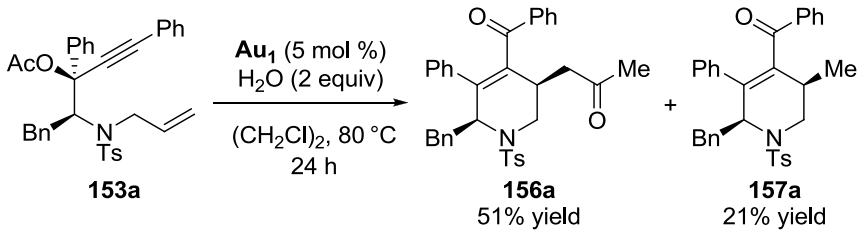
involves protodeauration that is a slower process than its equivalent generated from the starting material catalyzed by **Au_5**. The slower protodeauration process allowed the rotation of the oxonium C–C bond in the former N-heterocyclic adduct to give conformer **164'**, which minimize the unfavorable steric interactions between the acylium moiety and the aryl group (Scheme 2.5,path a). Subsequently, the Au–C(sp^3) bond acted as a nucleophile to attack the acyl carbonyl carbon center of the ester moiety via a 4-membered cyclic transition state, giving the resultant 1,5-acyl migration. The possibility of the rotation of the acyloxy group of a vinyl gold intermediate to facilitate the 1,5-acyl migration has also been supported by DFT calculations in Au(I)-catalyzed cycloisomerizations of 1,6-diyne acetates to δ-diketone substituted cyclopentenes.[47] In addition, a four-membered cyclic transition state has also been proposed in 1,3-acyl migration of an alkyl gold species formed in Au(I)-catalyzed dimerization of propiolic acids to 4-hydroxy-α-pyrones mentioned earlier[59] and that of a vinyl gold intermediate in Au(I)-mediated isomerization of propargylic acetates to α-ylidene-β-diketones.[69] The newly formed bicyclic gold intermediate **165** then produced **156**, releasing the gold(I) catalyst. The hypothesized rotation that results in the change of the conformation from **164** to **164'** that allows the 1,5-acyl shift involving nucleophilic attack of the Au–C(sp^3) bond to the acyl carbonyl carbon center to take place would be in line with earlier findings in our group showing **157a** obtained as the major product for the reaction of **153l** catalyzed by **Au_1**, and not **156l**. This is consistent with our postulate in which the rotation of the bond might be hindered by the bulky pivalate group, hence allowing the hydrolysis and protodeauration to take place. On the other hand, the corresponding alkyl gold **164** is

more susceptible to a simultaneous or stepwise hydrolysis process involving protodeauration in the presence of gold(I) phosphine complex **Au**$_5$ (Scheme 2.5, path b). With the addition of 2 equiv of water, the formation of **157** is achieved along with the carboxylic acid as a byproduct.



Scheme 2.5 Proposed mechanism for the cycloisomerization of **153** catalyzed by gold(I) complexes **Au$_1$** or **Au$_5$**.

The divergence in the azaheterocyclic products obtained in this study could be caused by the difference in the steric and electronic properties of the ligands in the gold(I) complex catalysts **Au$_1$** and **Au$_5$**. With reference to the study on the rate of protodeauration of various vinyl gold species conducted by Wang and co-workers in 2012, it was shown that gold(I) complex bearing a JohnPhos ligand demonstrated the fastest rate of protodeauration.[54] This was reasoned to be due to stabilization of the cationic gold complex via a η2-interaction of the ortho substituted phenyl ring along with the two bulky and electron-rich *t*Bu substituents on the phosphine center of the JohnPhos ligand. In the case of our present study, we believed that a similar ligand effect took place, in which the change in the catalyst from Au(I) phosphine complex **Au$_5$** to the NHC-gold(I) complex **Au$_1$** decreases the rate of protodeauration in **164**. Our hypothesis was further tested via a control experiment in which 1,7-enyne ester **153a** was subjected to the NHC-gold(I) complex **Au$_1$** in the presence of 2 equiv of H_2O under the conditions shown in Scheme 2.6. To our delight, δ-diketone adduct **156a** was obtained as the major product in 51% yield with the ketone product **157a** furnished in a low yield of 21% despite the presence of the proton source. This finding further supported our rationale that the ligand

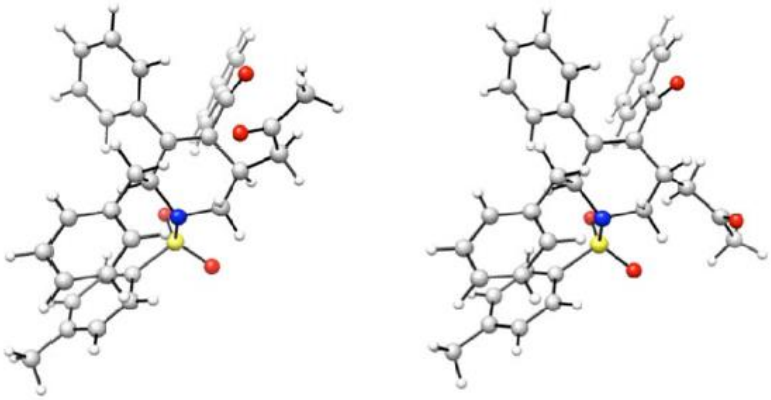


Scheme 2.6 NHC-gold(I) complex **Au$_1$** catayzed cycloisomerization of **153** in the presence of water

effect played an important role in the product divergency. The *cis* diastereoselectivity in the products have originated from the preferential conformation of the gold(I)-activated alkene **163** as shown in Scheme 2.5 prior to the azaheterocyclic ring formation process. This conformation kept the unfavorable transannular steric interactions between the substituents at its minimum during the cyclization to afford the nitrogen ring intermediate **165**. In addition, the formation of both azaheterocylic adducts as a single enantiomer from an enantiopure starting materials implied that no racemization occurred in the substrates or any of the intermediates. As a result, the enantioselectivity at the C3 position was observed through the efficient transfer of the retained chirality at the amino carbon center of the substrate.

Another possible source of the stereoselectivity observed in the transformation might be due to the thermodynamic control of the reaction. To study this, a density functional theory (DFT) calculation of the two possible isomers of **156a** was carried out. For each case, the Monte Carlo Multiple Minimum (MCMM) method as implemented in the MacroModel 9.9 program along with the use of the OPLS2005 force field was utilized to perform a conformational search in the gas phase.[70,71] The top 20 lowest-energy conformers for each isomer were then subjected to refined geometry optimizations at the B3LYP/6-31G* level.[72,73] Gaussian 09 and UCSF Chimera was used for the DFT calculations and to draw the molecules, respectively.[74,75] It was calculated that the most stable conformers of the two possible isomers of **156a**, *cis*-**2a** and *trans*-**2a**, have a similar relative energies of with the latter being slightly less stable by 0.73 kcal/mol (Figure 2.3). With an almost equal stability of the two isomers being obtained, the

possibility of thermodynamic control of the reaction was concluded to be unlikely.

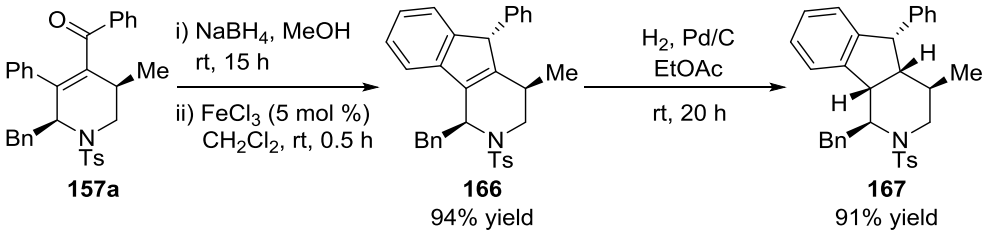


cis-**156a**	*trans*-**156a**
0.00	0.73

Figure 2.3 Most stable conformers of *cis*-**156a** and *trans*-**156a** (in kcal/mol) as obtained at the B3LYP/6-31G* level**.**

Having established an efficient methodology to access the *cis*-1,2,3,6-tetrahydropyridines, we applied this new approach to the synthesis of an enantiopure 2,3,4,4*a*,5,9*b*-hexahydroindeno[1,2-*c*]pyridine analogue (Scheme 2.7). The azaheterocycles bearing three rings are a class of compounds that is reported to exhibit biological activities such as antispermatogenic, antidepressant and antiintegrin activity.[61] Firstly, the ketone **157a** was reduced in room temperature with $NaBH_4$ in methanol. The resultant crude mixture was then treated with a mixture of 5 mol% of $FeCl_3$ in dichloromethane for 0.5 h affording the chiral 2,3,4,5-tetrahydro-1*H*-indeno[1,2-*c*]pyridine **166** in an excellent yield of 94% over two steps.[76] Lastly, a hydrogenation of

the newly formed tricyclic compound **166** in the presence of Pd/C in EtOAc furnished the desired 2,3,4,4*a*,5,9*b*-hexahydroindeno[1,2-*c*]pyridine **167** in 91% yield and as a single single diastereo- and enantiomer. An effective transfer of chirality was also observed for the 3-step transformations from the *cis*-1,2,3,6-tetrahydropyridine substrate **157a** to the desired product **167**. The stereochemistry of both **166** and **167** was assigned on the basis of NMR spectroscopic measurements via 2D NOESY spectroscopy.



Scheme 2.7 Synthesis of **167** from **157a**

2.3 Conclusion

In summary, we have described an efficient gold(I) catalyzed cycloisomerization of 1,7-enyne esters as a viable method for the synthesis of various *cis*-1,2,3,6-tetrahydropyridin-4-yl ketones and *δ*-diketones. The cycloisomerization to the formation of the *δ*-diketones product was speculated to involve a new type of 1,5-acyl migration of the acyl moiety to the Au–C(sp^3) unit. The synthetic methods were shown to be applicable to a various set of 1,7-enyne esters, providing stereochemically well-defined *cis*-1,2,3,6-tetrahydropyridines, which is a valuable scaffold found in natural products and pharmaceutical chemistry. Our studies showed by relying on the differences in the

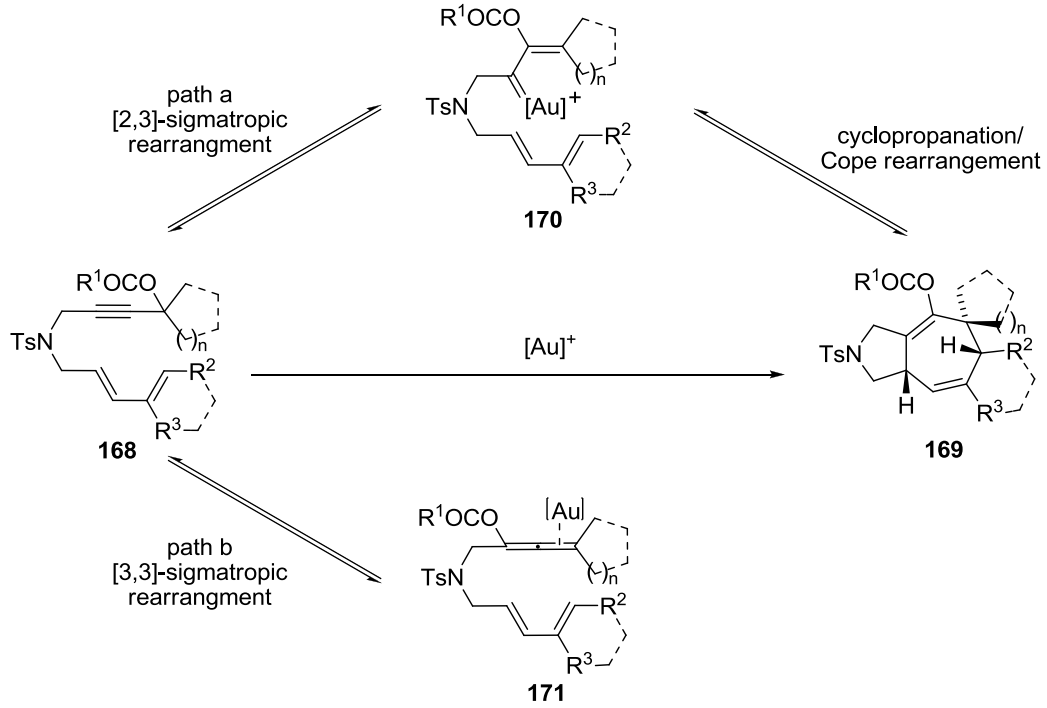
electronic and steric properties between a gold(I) phosphine catalyst and NHC-gold(I) complex and, an effective control of product selectivity was found to be feasible. The synthetic utility of this methodology to access these two classes of azaheterocycles was also demonstrated by synthesizing an enantiopure analogue of the bioactive 2,3,4,4*a*,5,9*b*-hexahydroindeno[1,2-*c*]pyridine family of compounds from one of the adduct obtained.

Chapter III. Gold Catalyzed Cycloisomerization of 1,6,8-Dienyne Carbonates and Esters to *cis*-Cyclohepta-4,8-diene-fused Pyrrolidines

3.1 Introduction

While cycloisomerization utilizing 1,*n*-enynes and 1,*n*-diynes have been widely explored in the last 20 years, those that make use of compound bearing two alkene moieties and an alkyne moiety, 1,*n*,*m*-dienynes, have been much less studied. Additionally, although other transition metal catalysts were described to be an efficient catalyst in catalyzing cycloisomerization of this type of compound, the use of gold catalysis was less explored with only one known example reported prior to this work[77-79] and no known studies on the reactivity of the carbonate and ester derivatives of these compounds. This is astonishing as the presence of another alkene moiety in the compound at an appropriate place could possibly open up a new type of transformation. We envisioned that the propensity of either a [2,3]- or [3,3]-sigmatropic rearrangement of the propargyl ester group would deliver either an allene or gold carbenoid adduct which could undergo further transformations similar to reactions involving [4+3] cycloaddition of allenedienes or a divinylcyclopropanation/ Cope rearrangement of gold carbenoid, respectively.[80-83] To our delight, we discovered that when 1,6,8-dienyne carbonates or esters **168** were subjected to gold(I) catalyst, *cis*-cyclohepta-4,8- diene-fused pyrrolidines **169** were obtained (Scheme 3.1). Added to this, it was observed that when R^2 = alkyl, a [2,3]-sigmatropic rearrangement occured followed by cyclopropanation and Cope rearrangement (Scheme 3.1, path a), while substrates bearing a terminal diene or

R^2 = Ph, a reversible [3,3]-sigmatropic rearrangement took place competitively (Scheme 3.1, path b). Although rare, the experimental evidence supporting the reversibility of [2,3]- and [3,3]-sigmatropic rearrangements in this field of gold catalysis were found.[84] It is also noteworthy that the divergence reaction pathways provided a single azacylic compound. This is unprecedented in gold-catalyzed cycloisomerization chemistry of propargylic esters in view of the fact that such initial rearrangements have been typically posited to dictate product selectivity. The *cis*-cyclohepta-4,8-diene-fused pyrrolidine ring structure is a potentially useful building block in organic synthesis as well as a valuable structural motif found in many pharmaceutical targets.[85] In addition, a new class of

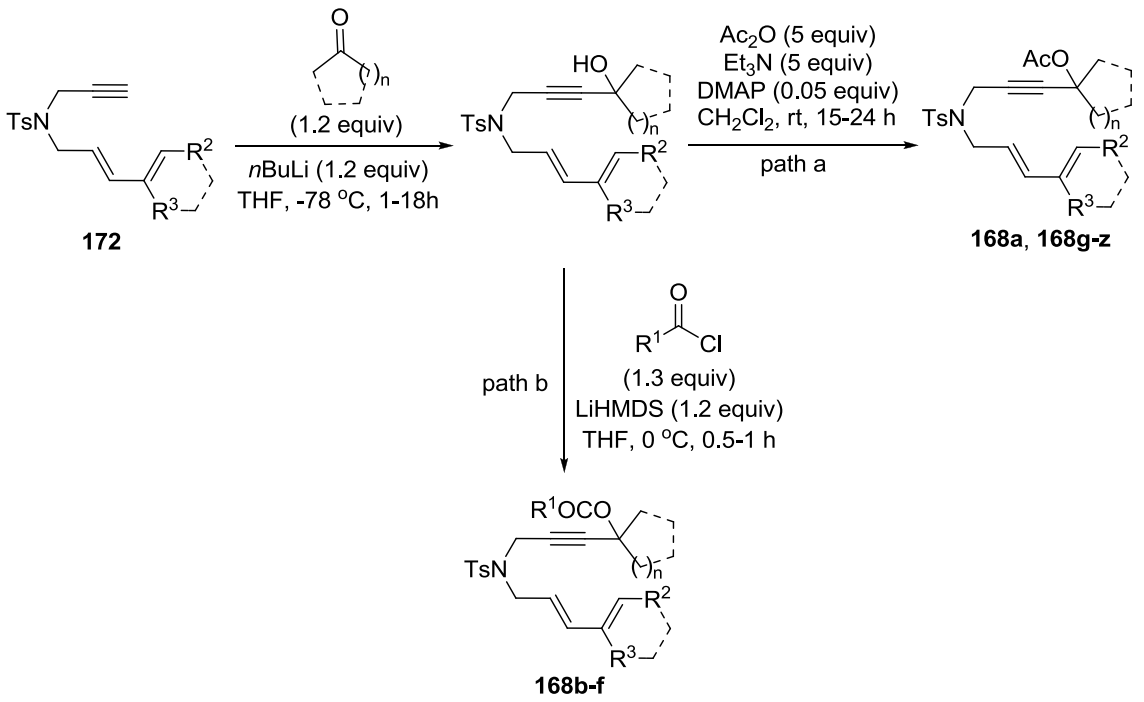


Scheme 3.1 Cycloisomerization of 1,6,8-dienyne carbonates and esters catalyzed by gold(I) catalysts

azaspirocyclic compounds could also be synthesized via this method under mild reaction conditions by altering the substituent on the starting 1,6,8-dienyne carbonates and esters to moeities bearing oxo- or carbocyclic rings.

3.2 Results and Discussion

The 1,6,8-dienyne carbonates and esters used in this work were prepared from (*E*)-4-methyl-*N*-(penta-2,4-dienyl)-*N*-(prop-2-ynyl)benzenesulfonamide **172** as shown in Scheme 3.2, with the latter being synthesized following literature procedures.[77-79] The 1,6-dienyne **172** obtained was subjected to *n*-butyllithium in tetrahydrofuran (THF) at -78 °C before a solution of a ketone was added to furnish 1,6,8-dienyne alcohols which,

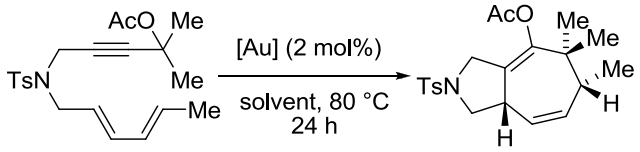


Scheme 3.2 Synthesis of 1,6,8-dienyne carbonate and esters **168**

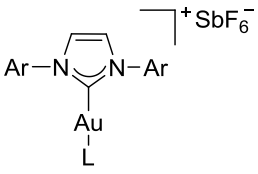
without characterization, were directly employed in the next reaction. Depending on the protecting group of the ester, two different methods of synthesis were employed. If the protecting group is an acetyl unit, the 1,6,8-dienyne alcohol was subjected to triethyl amine, 4-dimethylaminopyridine, acetic anhydride in dichloromethane to afford 1,6,8-dienyne ester **168a**, **168g-z** as depicted in Scheme 3.2, path a. On the other hand, if the protecting group is not an acetyl unit, LiHMDS was used as a base in THF with various acyl chlorides to furnish the respective 1,6,8-dienyne carbonates and esters **168b-f** (Scheme 3.2, path b).

Having obtained the starting material, our studies in optimizing reaction conditions were then started by utilizing 1,6,8-dienyne ester **168a** as model substrate (Table 3.1). An initial study revealed that subjecting **168a** to 5 mol% gold(I) phosphine catalyst $\mathbf{Au_5}$ in the presence of 4 Å molecular sieves with toluene as solvent at 80 °C for 24 h produced the *N*-heterocyclic product **169a** in 80% yield (entry 1). The structure of the cyclohepta-4,8-diene-fused pyrrolidine and the *cis* stereochemistry was confirmed by both ^{1}H,^{13}C NMR analysis and X-ray structure crystallography as depicted in Figure 3.1.[86] When the temperature of the reaction was reduced to room temperature, no formation of the *N*-heterocyclic product was formed, with the *cis*-cyclopropane **173a** obtained as a sole product in a high yield of 91% (entry 2). An analogous reaction without the presence of 4 Å molecular sieves as drying agent at 80 °C for 24 h furnished the azacylic adduct **169a** in an excellent yield of 99% (entry 3). Lowering the catalyst loading to 2 mol% resulted in slightly lower yield of 95% (entry 4). Repeating the reaction in the presence of $CaSO_4$ as drying agent in place of molecular sieves was found

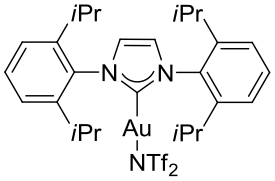
Table 3.1 Optimization of the reaction conditions[a]



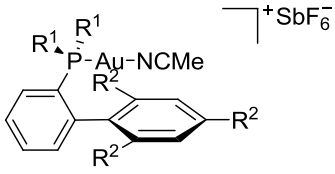
168a **169a**



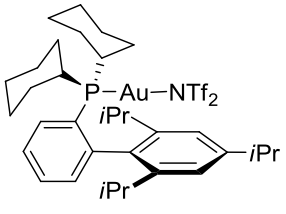
Au$_1$: Ar = 2,6-(*i*Pr)$_2$C$_6$H$_3$, L = PhCN
Au$_2$: Ar = 2,6-(*i*Pr)$_2$C$_6$H$_3$, L = DMAP
Au$_3$: Ar = 2,4,6-Me$_3$C$_6$H$_2$,
L = (2,4,6-(MeO)$_3$C$_6$H$_2$)CN



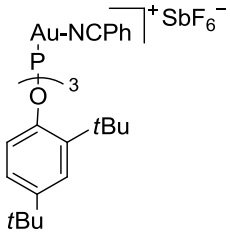
Au$_4$



Au$_5$: R^1 = *t*Bu, R^2 = H
Au$_6$: R^1 = *c*C$_6$H$_{11}$, R^2 = *i*Pr

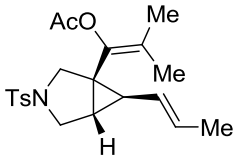


Au$_7$



Au$_8$

Au$_9$



173a

Entry	Catalyst	Solvent	Yield (%)[b]
1	**Au$_5$**[c]	PhMe	80
2[d]	**Au$_5$**	PhMe	-[e]
3	**Au$_5$**	PhMe	99[f]
4	**Au$_5$**	PhMe	95[f]
5[g]	**Au$_5$**	PhMe	95[f]
6	**Au$_5$**[h]	PhMe	68[f]
7	**Au$_5$**	1,4-dioxane	53
8	**Au$_5$**	$(CH_2Cl)_2$	85[f]

Table 3.1 *(continued).*

Entry	Catalyst	Solvent	Yield (%)[b]
9	**Au$_5$**	MeCN	14
10	**Au$_6$**	PhMe	69
11	**Au$_7$**	PhMe	29
12	$Ph_3PAuNTf_2$	PhMe	65
13	**Au$_8$**	PhMe	74
14	AuCl	PhMe	24
15	**Au$_1$**	PhMe	88[f]
16	**Au$_2$**	PhMe	12
17	**Au$_3$**	PhMe	67
18	**Au$_4$**	PhMe	44
19	**Au$_9$**	PhMe	24
20	$AuCl_3$	PhMe	28

[a] All reactions were carried out with 0.2 mmol of **168a** and 2 mol % of catalyst at 80 °C for 24 h. [b] ^{1}H NMR yield with dibromomethane (CH_2Br_2) as the internal standard. [c] Reaction carried out with 5 mol% of **Au$_5$** and 80mg of 4 Å MS. [d] Reaction carried out at room temperature. [e] Compound **173a** was isolated in 91% yield. [f] Isolated yield. [g] Reaction performed with 80 mg of $CaSO_4$. [h] Reaction performed with 1 mol% of **Au$_5$**.

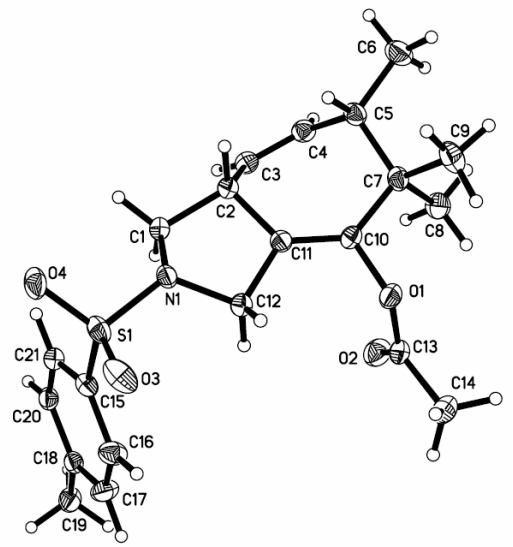


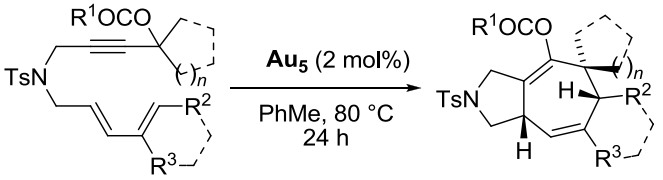
Figure 3.1 ORTEP drawing of *cis*-cyclohepta-4,8-diene-fused pyrrolidine **168a** with thermal ellipsoids at 50% probability levels

to furnish **169a** in comparable yield of 95% (entry 5). A decrease in the product yield to that of 68% was observed when 1 mol% catalyst loading was employed (entry 6). Subsequently, a screening of solvent was carried out in the presence of 2 mol% of gold(I) phosphine complex **Au$_5$** (entry 7-9). In general, lower product yields of 14-85% were obtained when the solvent was changed to 1,4-dioxane, 1,2-dichloroethane or acetonitrile. Having obtained the best catalyst loading of 2 mol% in toluene as solvent, a screening of different gold catalysts were performed (entries 10-20). The analogous reactions with gold(I) phosphine complex catalysts **Au$_6$**, **Au$_7$** and Ph_3PAuCl were found to give lower yields of 29-69% (entries 10-12). Other types of gold(I) catalysts such as gold(I) phosphite catalyst **Au$_8$** as well as simple gold(I) catalyst AuCl were also found to be ineffective in improving the product yield, giving **169a** in 74 and 24% yields,

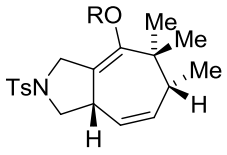
respectively (entries 13-14). Further subjecting 1,6,8-dienyne ester **168a** with NHC-Au(I) complexes **Au$_1$**-**Au$_4$** and gold(III) catalysts, **Au$_9$** and $AuCl_3$ gave **169a** in lower yields of 12-88% (entries 15-20). With the exception of the reaction with NHC-Au(I) **Au$_4$**, side products which were not able to be identified via NMR analysis were obtained in all other reactions. On account of the results obtained, the optimal reaction conditions of the cycloisomerization of **168a** were found to be 2 mol% of gold phosphine complex **Au$_5$** in toluene as solvent at 80 °C for 24 h.

We next turned to study the scope of this methodology by subjecting the optimum conditions onto various 1,6,8-dienyne carbonates and esters (Table 3.2). To our delight, this procedure was shown to be able to tolerate a range of 1,6,8-dienyne carbonates and esters **168b**-**z**, furnishing various *cis*-cyclohepta-4,8-diene-fused pyrrolidines **169b**-**z** in moderate to high yields of 41-81%. Substrates bearing different carbonates and esters moieties such as benzoyl (**168b**), *p*-nitrobenzoyl (**168c**), cyclobutyl carboxylate (**168d**), pivalate (**168e**) or carboxybenzyl (**168f**) groups were found to be well tolerated, giving the pyrrolidines **169b-f** in 49-84% yields. Altering the substituent next to the ester carbon center to bulkier cyclopentane (**168g**) and cyclohexane (**168h**) were shown to have no effect on the course of reaction, furnishing the corresponding spirocyclic adducts **169g** and **169h** in 82 and 65% yields, respectively. However, lower reaction temperature of 50°C was required when substrate bearing a cyclopentane ring as well as a propyl unit (**168i**) was involved in the transformation, giving the spirotricyclic adduct **169i** in 64% yield. The present procedure was also found to be effective for

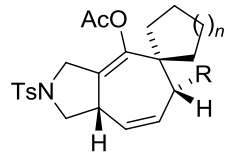
Table 3.2 Cycloisomerization of 1,6,8-dienyne **168b-z** catalyzed by $\mathbf{Au_5}$[a]



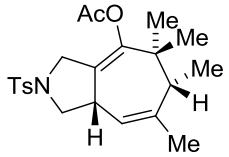
168 **169**



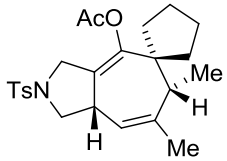
169b: R = Bz (71%)
169c: R = PNB (73%)
169d: R = C(O)cC_4H_7 (63%)
169e: R = Piv (84%)
169f: R = Cbz (49%)



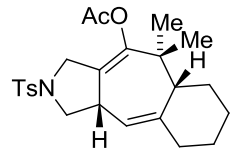
169g: R = Me, *n* = 1 (82%)
169h: R = Me, *n* = 2 (65%)
169i: R = *n*Pr, *n* = 1 (64%)[b]



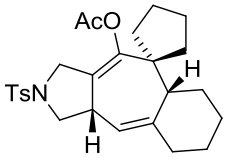
169j: (79%)



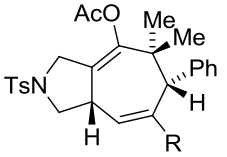
169k: (91%)



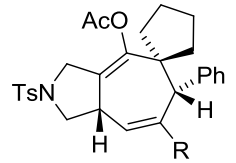
169l: (58%)



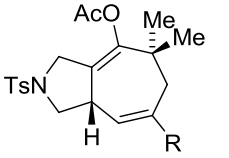
169m: (83%)



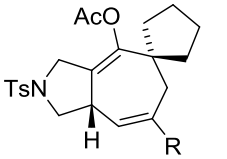
169n: R = Me (74%)
169o: R = *n*Hex (60%)



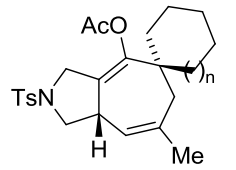
169p: R = Me (65%)
169q: R = *n*Hex (81%)



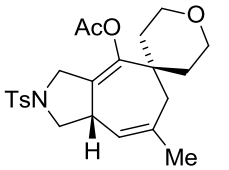
169r: R = H (74%)
169s: R = Me (72%)
169t: R = *n*Bu (77%)



169u: R = H (55%)
169v: R = Me (75%)
169w: R = *n*Bu (81%)



169x: n = 1 (58%)
169y: n = 2 (41%)[c]

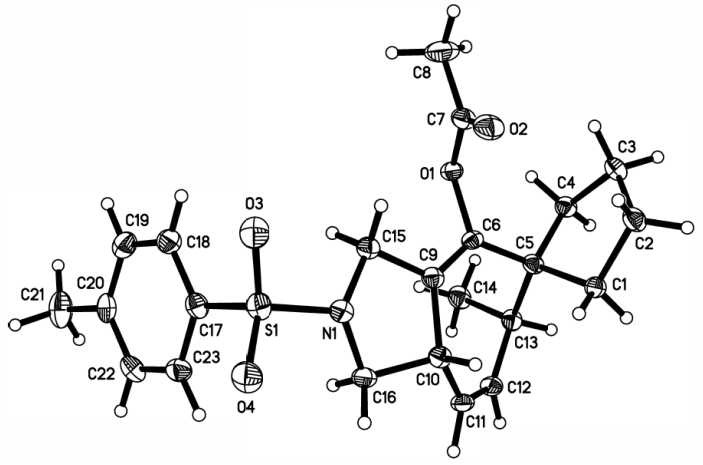


169z: (45%)

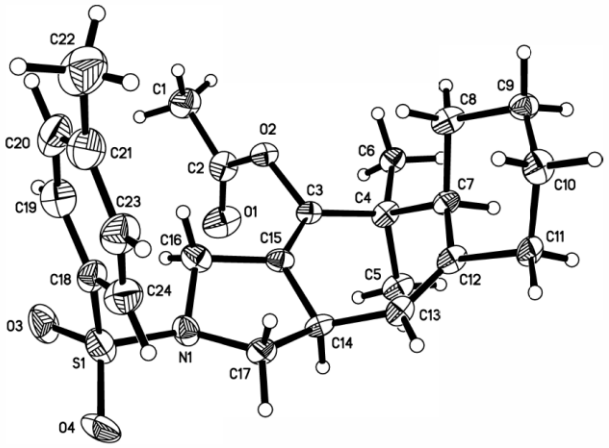
[a] Unless otherwise stated, all reactions were carried out at the 0.2 mmol scale with 2 mol% of $\mathbf{Au_5}$ at 80 °C for 24 h. Values in parentheses denote isolated product yields. [b] Reaction carried out at 50 °C. [c] Reaction was carried out for 48 h.

substrates containing different substituents on the 1,3-diene unit of the starting esters (**168j**-**168x** and **168z**). In general, the corresponding pyrrolidines **169j**-**169x** and **169z** were obtained in moderate to high yields of 45-91%. It is noteworthy that this included pyrrolidines bearing carbospiro- (**169k**, **169m**, **169 p**,**q** and **169 u**-**x**) or oxaspirocylic ring (**169z**), fused tricyclic ring system (**169l**) or tetracyclic system (**169m**). The only exception observed was when 1,6,8-dienyne ester bearing a cycloheptane ring **168y** was employed, longer reaction time of 48 h was needed for the complete consumption of the substrate to give the expected **169y** in 41% yield. While not listed in Table 3.2, the reaction of 1,6,8-dienyne ester containing oxygen instead of nitrogen tether have also been carried out under the optimized condition. However, the reaction did not proceed well with a mixture of unidentified decomposition products being obtained. Apart from this, the cycloisomerization of 1,6,8-dienyne carbonates and esters **168** were shown to be applicable to a wide range of substrates in a selective manner, giving the *cis* isomer of the cyclohepta-4,8-diene pyrrolidines adduct as a sole product. In addition, ^{1}H NMR analysis of the crude reaction mixtures shown that there are no other cycloadducts formed during the transformation process. X-ray crystal structures of **169g**, **169l** and **169v** were also obtained, further confirming the *cis* stereochemistry of the products (Figure 3.2).[87]

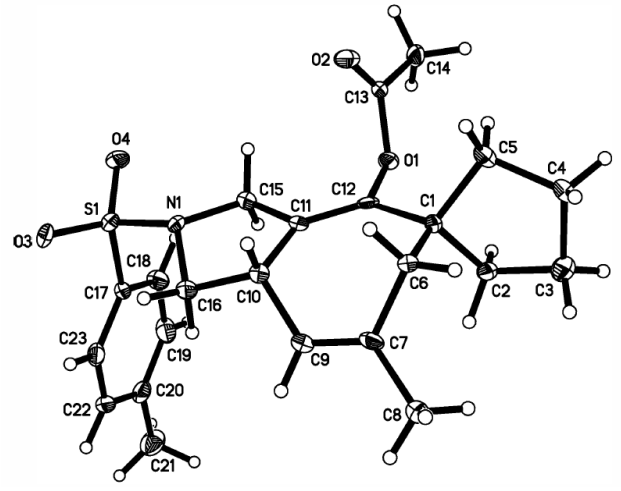
Next, we sought to study the mechanistic premise of the present transformation as depicted in Scheme 3.1 by conducting several control experiments. The isolation of *cis*-cyclopropane **173a** under certain conditions in the course of optimization studies (Table 3.1, entry 2) suggested that it might be an intermediate. To test this hypothesis, a control experiment was carried out by subjecting *cis*-cyclopropane **173a** in toluene



(a) **169g**



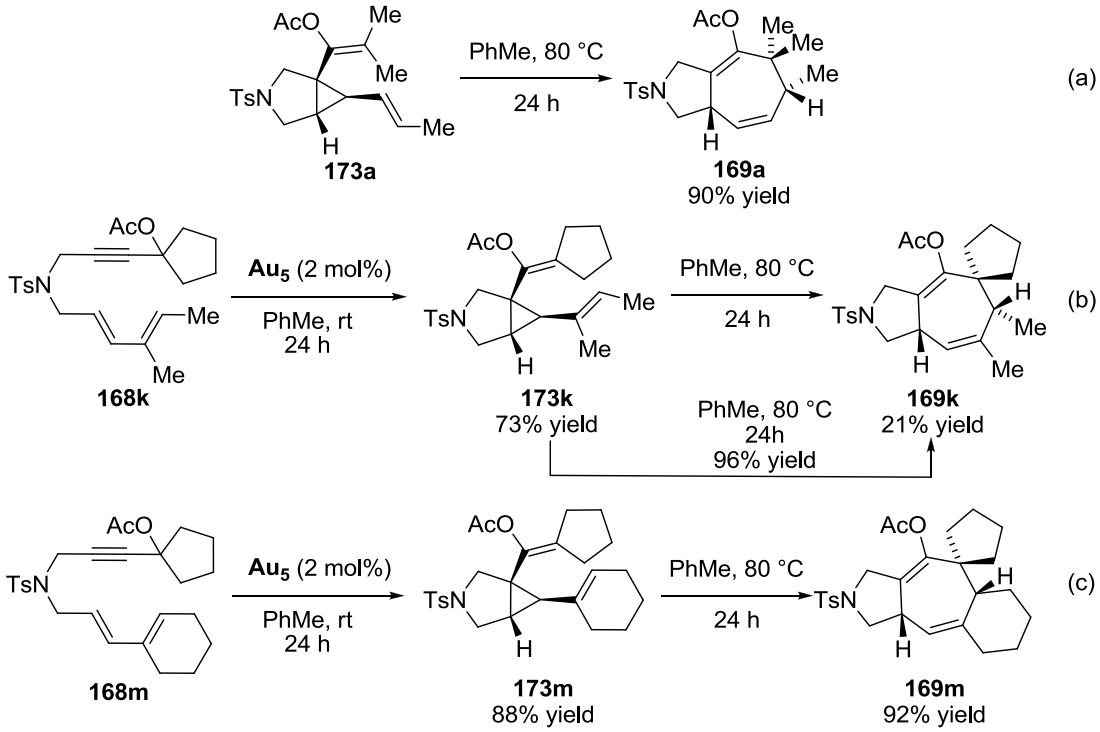
(b) **169l**



(c) **169v**

Figure 3.2 ORTEP drawings of **169g** (a), **169l** (b) and **169v** (c) with thermal ellipsoids at 50% probability levels

without the presence of gold(I) phosphine complex **Au_5** at 80 °C for 24 h (Scheme 3.3, eq a). To our delight, the *cis*-cyclohepta-4,8-diene pyrrolidine adducts **169a** was obtained in 90% yield, further confirming the cyclopropane **173a** as an actual intermediate. This was further supported by two other control experiments with **168k** and **168m**. When **168k** was treated with 2 mol% of **Au_5** in toluene at room temperature, cyclopropane adduct **173k** was obtained in 73% yield along with **169k** in 21% yield (Scheme 3.3, eq b). Likewise, when **168m** was subjected to the same reaction conditions, **173m** was obtained in 88% yield (Scheme 3.3, eq c). Further treatment of the *cis*-6-vinyl-3-azabicyclo[3.1.0]hexane adducts **173k** and **173m** in toluene at 80 °C for 24 h

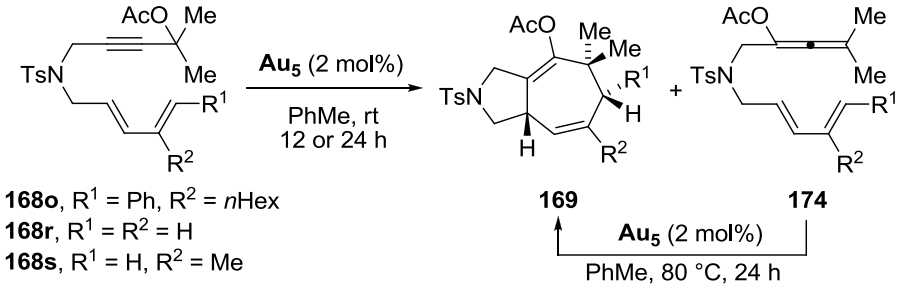


Scheme 3.3 Control experiments with **173a** under thermal conditions (a), **168k** and **168m** (b and c) catalyzed by gold(I) phosphine catalyst **Au_5**

furnished the corresponding *N*-heterocyclic products **169k** and **169m** in high yields of 96 and 92%, respectively (Scheme 3.3, eq b and c). In addition, the formation of the products without the presence of any gold catalysts implied that a thermal Cope rearrangement took place.[82,87]

In the course of our studies, we found that the gold(I) phosphine catalyst **Au_5** catalyzed cycloisomerization of 1,6,8-dienyne ester **168s** in room temperature for 12 h afforded the pyrollidine product **169s** in 24% yield and an inseperable mixture of allenic acetate **174s** and unreacted 1,6,8-dienyne ester **168s** in a ratio of 5.5:1 in 63% yield (Table 3.3, entry 5). This prompted us to carry out several control experiments to investigate the involvement of allenic acetates **174** in our present procedure (Table 3.3). The same reaction was carried out for a longer reaction time of 24 h and it was found to afford **169s** in 61% yield and **174s** in lesser yield of 28% (entry 6). While not listed in Table 3.3, the inseparable mixture of **168s** and **174s** was found to be resistant to undergo further transformation in toluene at 80 °C for 24 h without the presence of **Au_5**. The utility of Au(I) catalyst in the transformation was further corroborated when the conversion of the allenic acetate **174s** to the pyrrolidine product **169s** was only observed when the reaction was carried out in the presence of gold(I) phosphine complex **Au_5** (entry 7). Similar findings were also found when **168o** and **168r** were subjected to the same reaction conditions (entries 1-4). Treatment of **168o** in the presence of **Au_5** at room temperature for 24 h produced the *N*-heterocyclic compound **169o** in 18% yield along with **174o** and **168o** in 5:1 ratio as an inseparable mixture in 70% yield (entry 1). On the other hand, **169r** was obtained in 21% yield along with an inseparable mixture of **174r**

Table 3.3 Control experiments with **168o**, **168r** and **168s** in the presence of $\mathbf{Au_5}$[a]



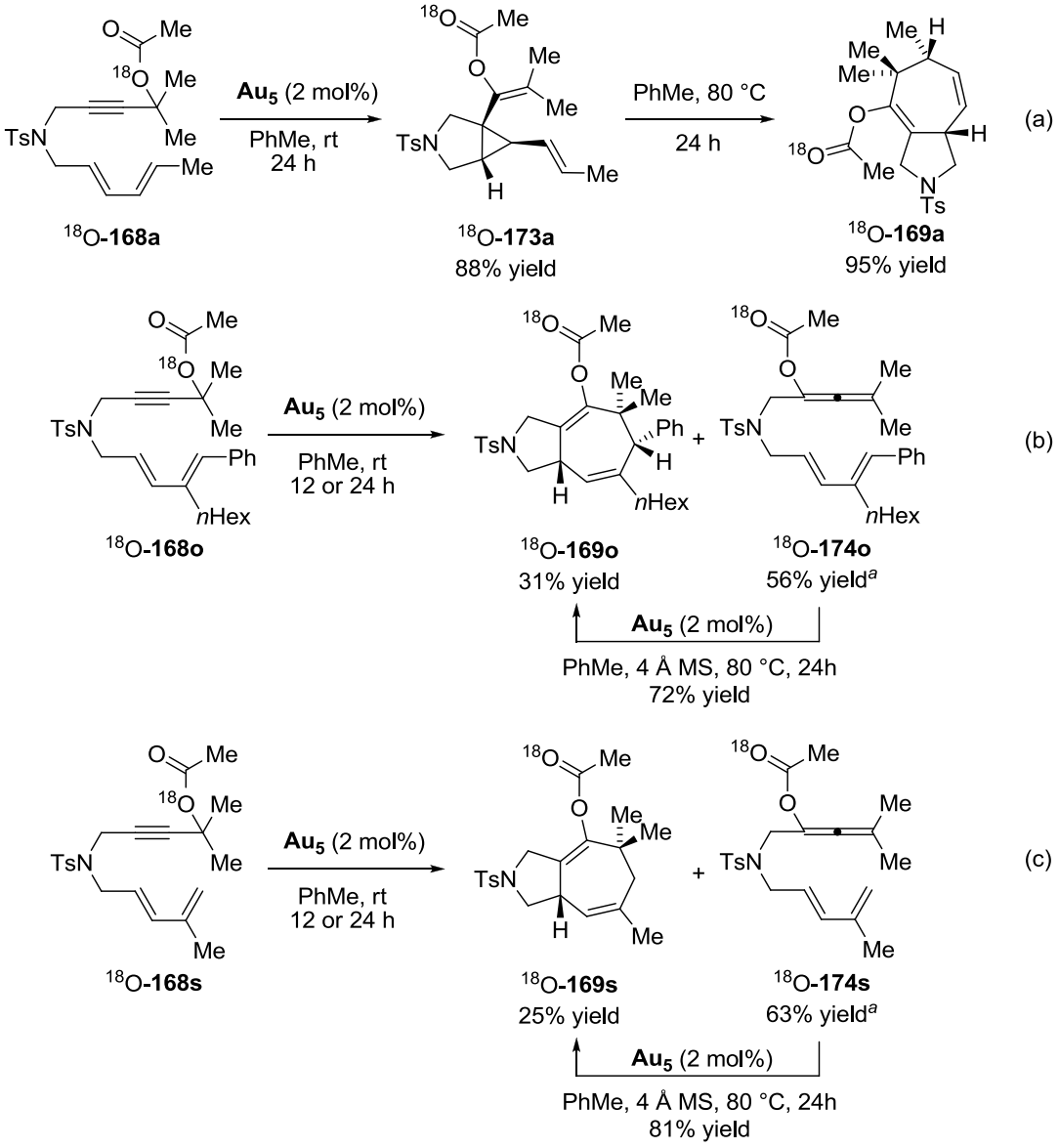
Entry	Substrate	Product	Yield (%)[b]
1	**168o**	**169o**	18
		168o + **174o**	70 (1:5) [c]
2[d]	**168o** + **174o** (1:5) [c]	**169o**	72
3	**168r**	**169r**	21
		168r + **174r**	51 (1:4) [c]
4[d]	**168r** + **174r** (1:4) [c]	**169r**	71
5[e]	**168s**	**169s**	24
		169s + **174s**	63 (1:5.5) [c]
6	**168s**	**169s**	61
		174s	28
7[d]	**168s** + **174s** (1:5.5) [c]	**169s**	79

[a] All reactions were performed with 0.2 mmol of **168**, 2 mol% of $\mathbf{Au_5}$ and 100mg of 4Å MS at room temperature for 24 h. [b] Isolated yield. [c] Values in parentheses denote the ratio of **168**:**174** based on ^{1}H NMR analysis. [d] Reaction performed at 80 °C for 24 h. [e] Reaction time = 12 h.

and **168r** in 4:1 ratio at 51% yield (entry 3). In both cases, the inseparable mixtures of **168o** + **174o** and **168r** + **174r** were shown to give the corresponding *cis*-cyclohepta-4,8-diene pyrrolidines **169o** and **169r** in 72 and 71% yield, respectively, in the presence of gold(I) phosphine complex at 80 °C for 24 h (entries 2 and 4). On the basis of results obtained in this set of control experiments, we deduced that substrates bearing terminal alkene moiety or Ph unit at the alkenyl carbon center could have possibly undergone transformations involving a [3,3]-sigmatropic rearrangement of the propargylic carbonate or ester moiety.

In order to gain a better understanding on the initial [2,3]- or [3,3]-sigmatropic pathways, last set of control experiments with ^{18}O-labeled analogues of **168a**, **168o** and **168s** were carried out (Scheme 3.4). The determination of the position of the ^{18}O-labeled atom in all of the compounds was done via the different stretching frequencies of the C=O and C-O as compared to that of C=O^{18} and C-O^{18} bond in FTIR spectroscopy. Under the reaction conditions depicted in Scheme 3.4, eq a, ^{18}O-**168a** was found to give the corresponding *cis*-cyclopropane intermediate ^{18}O-**173a** in a high yield of 88%. Further transformation took place when the newly formed intermediate was heated at 80 °C for 24 h in toluene, affording the corresponding *N*-heterocyclic product ^{18}O-**169a** in 95% yield. Similarly, subjecting ^{18}O-**168o** to gold(I) phosphine complex **Au$_5$** in toluene at room temperature was found to furnish ^{18}O-**169o** in 31% yield and an inseparable mixture of ^{18}O-**174o** and unreacted ^{18}O-**168o** in 5:1 ratio in 56% yield (Scheme 3.4, eq b). Reaction of ^{18}O-**168s** was also found to give a similar result with ^{18}O-**169s** obtained in 25% yield and an inseparable mixture of allenic acetate ^{18}O-**174s**

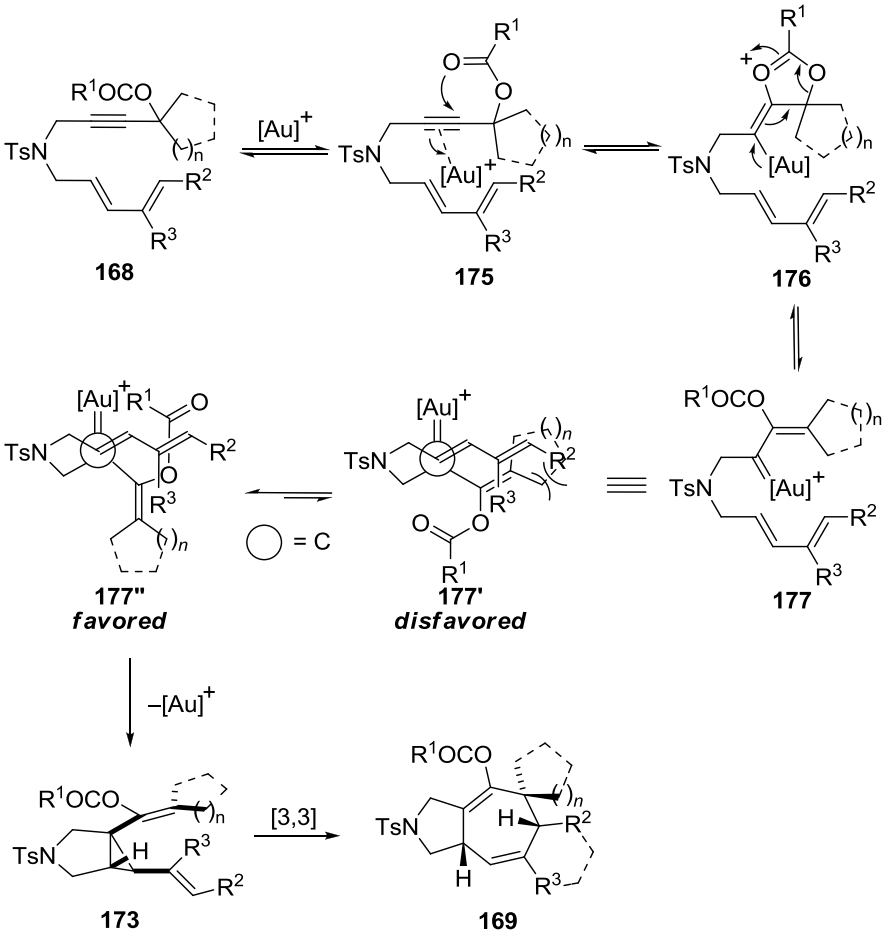
and the starting ^{18}O-**169** in the ratio of 5:1 in 63% yield (Scheme 3.4, eq c). When the mixtures of ^{18}O-**168o** +^{18}O-**174o** and ^{18}O-**168s** + ^{18}O-**174s** were subjected to gold(I) complex **Au$_5$** as catalyst at 80 °C for 24 h in toluene as a solvent, the corresponding



Scheme 3.4 Control experiments with ^{18}O-**168a**, ^{18}O-**168o** and ^{18}O-**168s**. [a] Product yield refers to inseparable mixture of the allenic ester and starting material in 5:1 ratio.

pyrrolidines ^{18}O-**169o** and ^{18}O-**169s** were obtained in 72 and 81% yield, respectively (Scheme 3.4, eq b and c). On the basis of the results obtained, we surmised that a reversible [2,3]- and [3,3]-sigmatropic rearrangement of the propargyl ester group of the 1,6,8-dienyne esters was involved in the present transformation.

Plausible mechanisms for the current procedure were proposed based on the findings above (Scheme 3.5 and 3.6). As depicted in Scheme 3.5, an initial activation of the

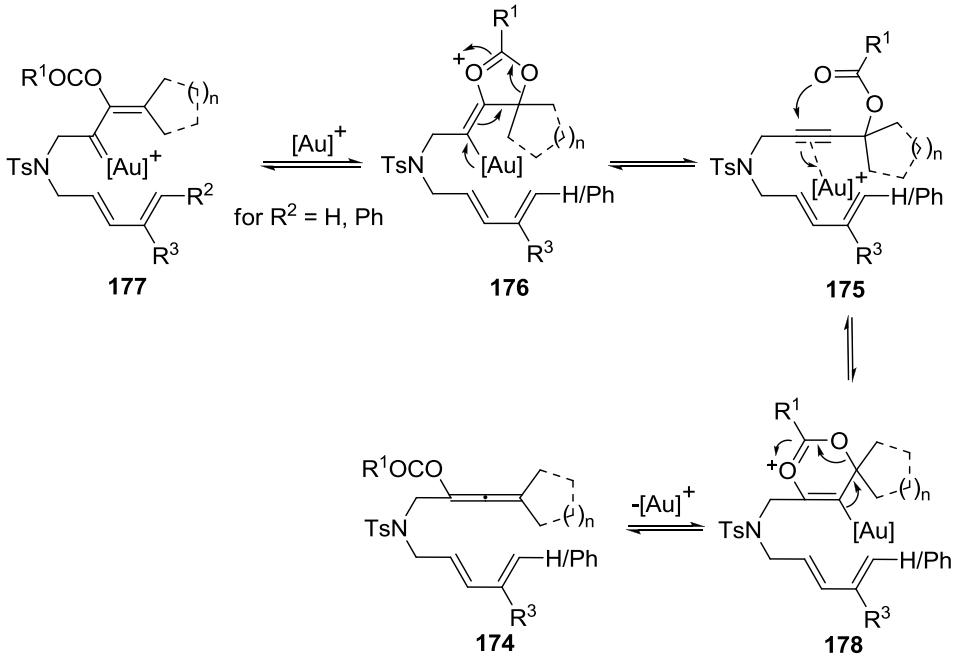


Scheme 3.5 Proposed mechanism for **Au$_5$**-catalyzed [2,3]-sigmatropic rearrangement/ cyclopropanation and thermal Cope rearrangement of **168** where R^2 = alkyl.

alkyne moiety by the gold(I) catalyst give the gold(I) coordinated complex **175**. Subsequently, a facile [2,3]-sigmatropic rearrangement of the carbonate or ester moiety took place to give the gold carbenoid adduct **177** via 1,3-dioxin-1-ium intermediate **176**. The newly formed putative gold carbenoid **177** may adopt the conformation **177"** over that of **177'** so as to minimize the unfavourable steric interactions between the substituents on the distal alkene bond of the diene moiety and vinyl carbonate or ester unit. This conformation allowed the organogold adduct to be trapped by the proximal C=C bond of the remaining diene group in *syn* manner to furnish the *cis*-cyclopropane **173** along with the regeneration of the Lewis acidic catalyst. Thermal Cope rearrangement of the newly formed *cis*-1,2-divinylcyclopropane **173** would then take place to give the *cis*-cyclohepta-4,8-diene pyrrolidines product **169**.[87-89]

For substrates where R^2 = H or Ph, the cyclopropanation of **177** to **173** is thought to be less efficient. This might be due to the less π-rich nature of the diene unit in gold(I) carbenoid adduct **177**, which led the equilibrium to shift and favour the formation of the gold(I)-activated species **175** (Scheme 3.6).[84] Subsequent [3,3]-sigmatropic rearrangement of this species via the 1,3-dioxin-1-ium intermediate **178** would then give the allenic ester **174** along with the regeneration of the gold(I) complex catalyst. It is noteworthy that a preferential initial [3,3]-sigmatropic rearrangement could have possibly taken place for substrate with R^2 = alkyl groups. However, the allenic ester formed would be resistant to undergo [4+3] cycloaddition, causing cycloreversion to occur. In such, a resultant [2,3]-sigmatropic rearrangement would eventually took place to give the corresponding product. In addition, the isolation of allenic carbonate or ester could be

due to its stability as compared to the strained cyclopropane intermediate.



Scheme 3.6 Proposed mechanism for **Au_5**-catalyzed formation of **174** for substrates in which R^2 = H, Ph

3.3 Conclusion

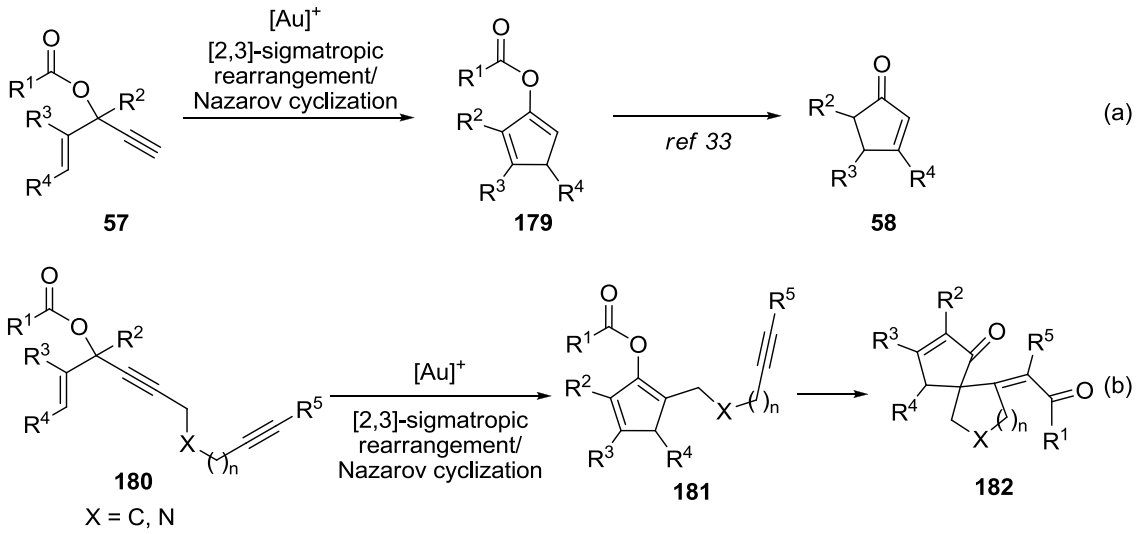
In summary, an efficient and selective Au(I)-catalyzed cycloisomerization of 1,6,8-dienyne carbonates and esters to access a range of *cis*-cyclohepta-4,8-diene-fused pyrrolidines was described. This methodology was also shown to be able to access compounds containing spirocyclic moiety from substrates bearing a pendant ring motif at the carbonyl carbon center. Depending on the substitution pattern on the distal alkene unit of the diene moiety, the corresponding *cis*-cyclopropane or allenic ester could be obtained. This served as an evidence of the oft-proposed reversibility of [2,3]- and [3,3]-

sigmatropic rearrangement. The formal gold(I)-catalyzed [4C+3C] cycloaddition approach represents an attractive alternative to previously reported metal-catalyzed reactions both in terms of atom economy and functional group tolerance.

Chapter IV. Gold Catalyzed Cycloisomerizations of 1-Ene-4,*m*-Diyne Esters: A Route to Prepare Spirocyclic Compounds

4.1 Introduction

Synthetic methodology relying on the use of unsaturated precursors such as 1,*n*-enyne and 1,*n*-diyne carbonates and esters with Lewis acidic gold catalysts, such as those described in Chapter I, Section 1.4 and 1.5 have been studied extensively due to the atom economical nature of the reactions. Recently, we delineated one example that shared gold(I) complex catalyzed cycloisomerization of unsaturated carbonate and ester compounds bearing one alkyne unit and two alkene moieties (Chapter III). However, to our knowledge, there are no known examples of studies on gold catalysis involving carbonate or ester compounds bearing two alkyne groups and one alkene unit. This is surprising as an appropriately placed alkene moiety on 1,*n*-diyne motif could possibly open novel methodology for the synthesis of cyclic compounds. By tapping on the propensity of 1,4-enyne carbonates or esters to undergo a preferential initial [2,3]-sigmatropic rearrangement of the carbonate or ester unit of the substrate to give the highly reactive gold(I)-pentadienyl cation-like compound, which subsequently could undergo a metallo-Nazarov cyclization to form cyclopentadiene intermediate **179**, as shown in Scheme 4.1,[90,91] we envisioned that further transformation could possibly occur with the presence of a pendant alkyne moiety in this newly formed intermediate. With this in mind, we designed 1-ene-4,*m*-diyne esters **180** and discovered that upon subjecting this substrate to a gold(I) complex catalyst, a range of spiro[4.*n*]-ketones **182** were



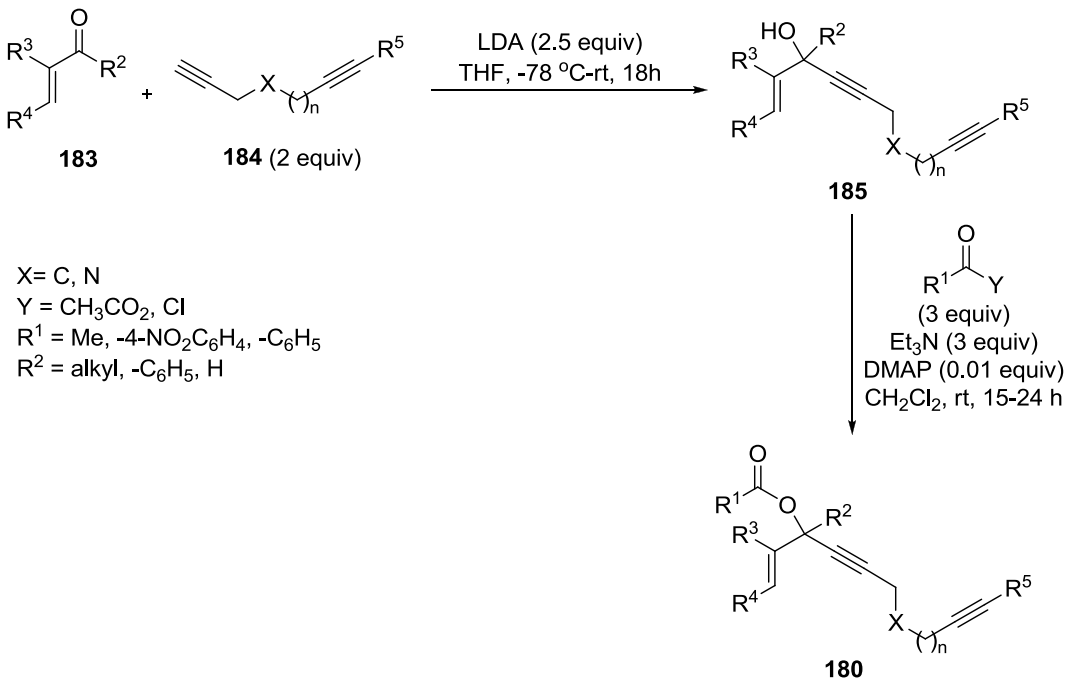
Scheme 4.1 Gold(I) mediated cycloisomerization of 1-ene-4,*m*-diyne esters to spirocyclic compounds

obtained via the cyclopentadiene intermediate **181** (Scheme 4.1). As a part of ongoing studies in gold catalysis in our group,[60] we describe herein this chemistry that offers an expedient route to the synthesis of spiro[4.*n*]-ketone, which is a structural motif found in several biologically active compounds.[1g-1i] Additionally, this methodology is also shown to be potentially useful for the synthesis of other types of cyclic compounds.

4.2 Results and Discussion

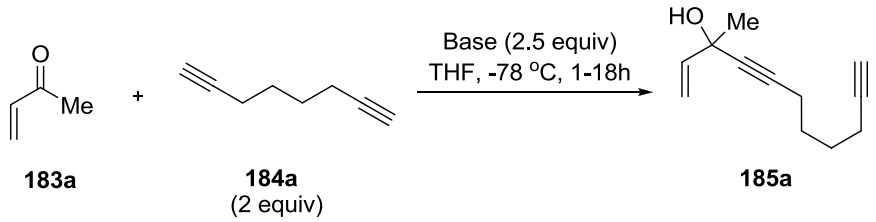
The 1-ene-4,*m*-diyne esters **180** used in this work were prepared via two different methods, as shown in Scheme 4.2 and 4.3. One of the synthetic methods, depicted in Scheme 4.2, made use of α,β-unsaturated ketones or aldehydes **183** and 1,*n*-diynes **184** that were prepared following literature procedures.[92-93] The reaction of ketone **183** with 1,*n*-diyne **184** in the presence of a base was found to give low yields of the alcohol **185**,

which prompted us to carry out a simple optimization study using ketone **183a** and 1,7-octadiyne **184a**, as shown in Table 4.1. The best yield of 38% of the corresponding alcohol **185a** was found to be achieved when LDA was used as a base (entry 1). Repeating the reaction with another base such as *n*-butyllithium was found to be ineffective, giving trace amount of product (entry 2). Other bases were also shown to be unsuccessful, furnishing the desired alcohol in lower yields of 8-16% (entry 3-5). Subsequent protection of the alcohol obtained with 3 equiv of either acetic anhydride or *p*-nitrobenzoyl chloride or benzoyl chloride in the presence of 3 equiv of triethyl amine, 0.01 equiv of DMAP in dichloromethane as a solvent for 15-24 h furnished the corresponding 1-ene-4,*m*-diyne esters **180a-d** and **180g-m** quantitatively.



Scheme 4.2 Synthesis of 1-ene-4,*m*-diyne esters **180a-d** and **180g-m** from α,β-unsaturated ketones or aldehydes **183**

Table 4.1 Optimization of α,β-unsaturated ketones **183** with diynes **184**[a]

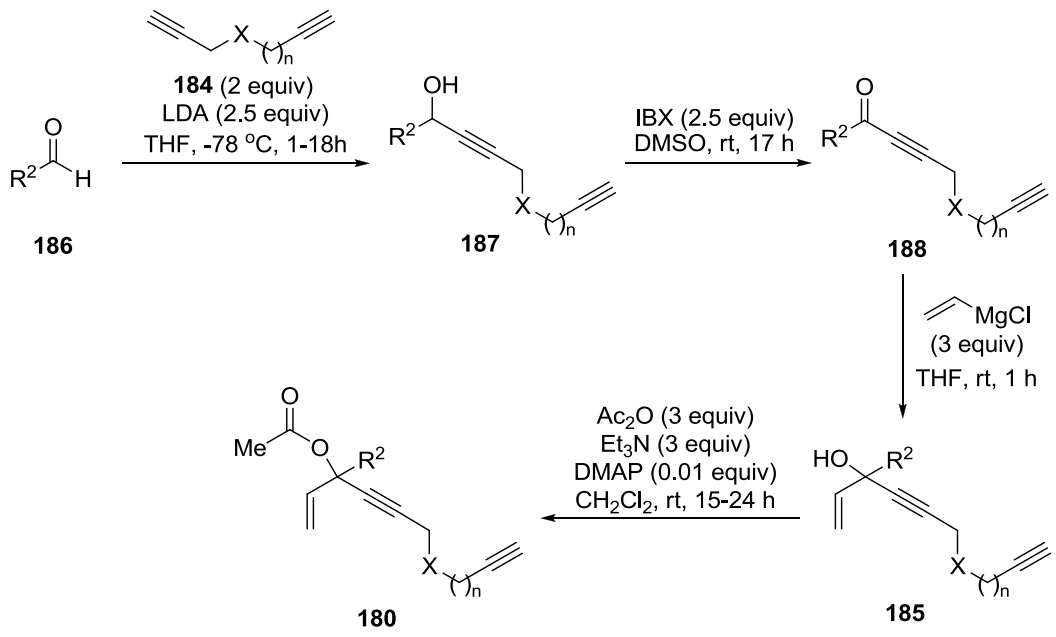


183a **184a** (2 equiv) **185a**

Entry	Base	Yield (%)[b]
1	LDA	38
2	*n*BuLi	-
3	KHMDS	8
4	NaHDMS	10
5	LiHMDS	16

[a] All reactions were carried out with 2 mmol of **183a** and 4 mmol **184a** with 2.5 equiv of base in THF at -78 °C for 1-18 h. [b] Isolated yield.

A different route was employed to prepare 1-ene-4,*m*-diyne esters **180e** and **180f**. As depicted in Scheme 4.3, aldehydes **186** were employed instead of α,β-unsaturated ketones. Nucleophilic addition of diyne **184** to the aldehyde with LDA as base in THF at -78 °C provided alcohols **187** which upon oxidation by IBX in dimethyl sulfoxide as a solvent furnished the corresponding ketones **188**. The reaction of ketone **183** with 3 equiv vinyl magnesium chloride in THF for 1 h produced alcohol **185**, which subsequently protected with acetate group to form 1-ene-4,*m*-diyne esters **180e** and **180f**.

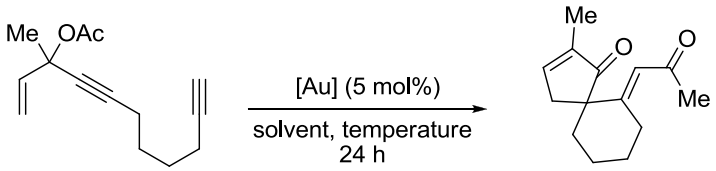


Scheme 4.3 Synthesis of 1-ene-4,*m*-diyne esters **180e** and **180f** from aldehydes **186**

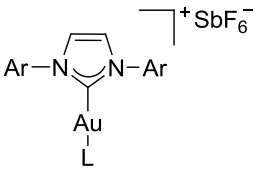
With 1-ene-4,10-diyne ester **180a** as the model substrate, we began our study to find the optimum reaction conditions for this transformations (Table 4.2). An initial study showed that in the presence of 5 mol% gold(I) phosphine complex **Au$_5$** and 4Å MS in toluene at room temperature for 24 h, (*E*)-2-methyl-6-(2-oxopropylidene)spiro[4.5]dec-2-en-1-one **182a** was obtained in 75% yield (entry 1). Repeating the reaction with slightly bulkier gold(I) phosphine complex **Au$_6$** and gold(I) phosphine complex with different counter ion **Au$_7$** gave the corresponding spiro compound in a lower yield of 73 and 29% (entries 2 and 3). Simpe gold catalysts such as AuCl, AuCl/$AgSbF_6$, $AuCl_3$/$AgSbF_6$ and gold(I) phosphine **Au$_8$** were shown to be unable to furnish the desired product, with mixture of unidentified products obtained (entries 4-7). Further screening of other catalysts such as NHC-gold(I) complexes **Au$_1$** and **Au$_4$** were found to be ineffective, giving moderate yields of 58 and 47%, respectively (entries 8 and 9). Reactions with

gold(III) complex **Au_9**, gold phosphate **Au_{10}** with $AgSbF_6$ co-catalyst and NHC-gold(I) complex with tetrafluoroborate anion **Au_{11}** were also found to give low product yields of 11-21% yields (entries 10-12). It was also found that reactions with $AuCl/AgSbF_6$ and gold(III) complex **Au_9** furnished cyclopentadiene **181a** in 21 and 51% yield, respectively. No reaction was observed when 1-ene-4,10-diyne ester **180a** was subjected to $AgSbF_6$ as catalyst without the presence of gold(I) catalyst (entry 13). Repeating the reaction without 4 Å MS or with $CaSO_4$ as a drying agent was found to be ineffective, furnishing no product and low yield of 35%, respectively (entries 14 and 28). Increasing the temperature of the reactions to 80 °C was found to decrease the formation of the product to 57-58% yields (entries 15 and 16). Decreasing the temperature to 50 °C while varying the reaction time were found to improve the reaction to give the highest yield of spirocyclic product of 89% (entry 18). Changing the solvents to other solvents such as tetrahydrofuran and acetonitrile were found to give no desired product (entries 19 and 20). On the other hand, reaction in dichloromethane was found to give the product in 50% yield with sign of decomposition observed via TLC analysis (entry 21). Repeating the reaction in CH_2Cl_2 at room temperature was found to decrease the decomposition while increase the yield of **182a** to 71% (entry 22). However, upon changing the solvent to 1,2-dichloroethane, the reaction was found to furnish the spiro adduct in 68% yield (entry 23). Upon examination of the catalyst loading of this reaction by altering the loading to 1, 3, 8 and 10 mol%, it was found that the spirocyclic product was obtained in lower yields of 10-78% (entries 24-27). Hence, the optimum condition of present cycloisomerization is 5 mol% of gold(I) phosphine complex **Au_5** with 4 Å MS at 50 °C in toluene for 24 h.

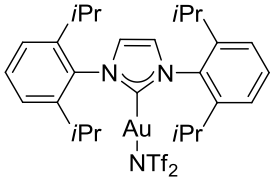
Table 4.2 Optimization of the reaction conditions[a]



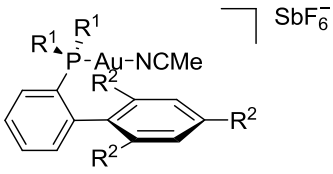
180a **182a**



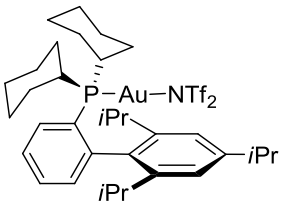
Au$_1$: Ar = 2,6-(*i*Pr)$_2$C$_6$H$_3$, L = PhCN



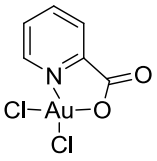
Au$_4$



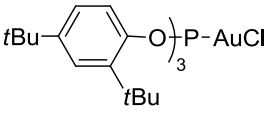
Au$_5$: R^1 = *t*Bu, R^2 = H
Au$_6$: R^1 = *c*C$_6$H$_{11}$, R^2 = *i*Pr



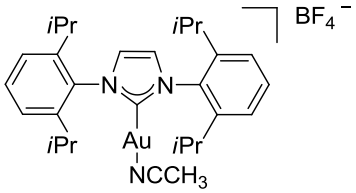
Au$_7$



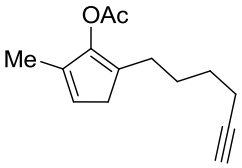
Au$_9$



Au$_{10}$



Au$_{11}$



181a

Entry	Catalyst	Temperature (°C)	Solvent	Yield (%)[b]
1	**Au$_5$**	rt	PhMe	75[c]
2	**Au$_6$**	rt	PhMe	73[c]
3	**Au$_7$**	rt	PhMe	29
4	AuCl	rt	PhMe	-[d]
5	AuCl/AgSbF$_6$	rt	PhMe	-[e]
6	AuCl$_3$/AgSbF$_6$	rt	PhMe	-[d]

Table 4.2 *(continued.)*

Entry	Catalyst	Temperature (°C)	Solvent	Yield (%)[b]
7	PPh_3AuNTf_2	rt	PhMe	-[d]
8	**Au$_1$**	rt	PhMe	58
9	**Au$_4$**	rt	PhMe	47
10	**Au$_9$**	rt	PhMe	-[f]
11	**Au$_{10}$**/$AgSbF_6$	rt	PhMe	21
12	**Au$_{11}$**	rt	PhMe	11
13	$AgSbF_6$	rt	PhMe	-[g]
14[h]	**Au$_5$**	rt	PhMe	48
15	**Au$_5$**	80	PhMe	58
16	**Au$_5$**	80	PhMe	57[i]
17	**Au$_5$**	50	PhMe	63[j]
18	**Au$_5$**	50	PhMe	89
19	**Au$_5$**	50	THF	-[k]
20	**Au$_5$**	50	CH_3CN	-[k]
21	**Au$_5$**	50	CH_2Cl_2	50
22	**Au$_5$**	rt	CH_2Cl_2	71[c]
23	**Au$_5$**	rt	$(CH_2Cl)_2$	68
24[l]	**Au$_5$**	50	PhMe	10[k]
25[m]	**Au$_5$**	50	PhMe	78[c]

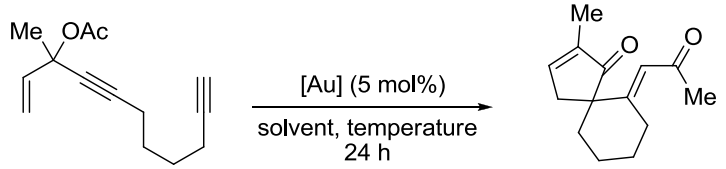
Table 4.2 *(continued.)*

Entry	Catalyst	Temperature (°C)	Solvent	Yield (%)[b]
26[n]	**Au$_5$**	50	PhMe	78[c]
27[o]	**Au$_5$**	50	PhMe	71
28	**Au$_5$**	50	PhMe	35[p]

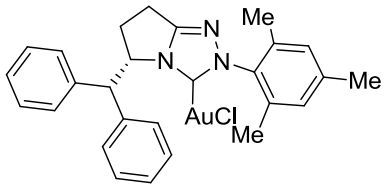
[a] All reactions were carried out with 0.2 mmol of **180a**, 5 mol % of catalyst and 80mg of 4Å MS at rt for 24 h. [b] ^{1}H NMR yield with dibromomethane (CH_2Br_2) as the internal standard. [c] Isolated yield. [d] Mixture of unidentified products, product, starting material and intermediate. [e] Cyclopentadiene **181a** obtained in 21% yield with 20% of starting material recovered. [f] Cyclopentadiene **181a** obtained in 51% yield. [g] No reaction based on ^{1}H NMR analysis of the crude mixture. [h] Reaction carried out without 4 Å MS. [i] Reaction carried out for 3 h. [j] Reaction carried out for 5 h. [k] Starting material recovered in 40% yield. [l] Reaction carried out with 1 mol% of [Au]. [m] Reaction carried out with 3 mol% of [Au]. [n] Reaction carried out with 8 mol% of [Au]. [o] Reaction carried out with 10 mol% of [Au]. [p] Reaction carried out with 80mg of $CaSO_4$.

An attempt to develop an enantioselective version of the present work was also been carried out. In our hands, this transformation was found to be unable to give (*E*)-2-methyl-6-(2-oxopropylidene)spiro[4.5]dec-2-en-1-one **182a** enantioselectively with gold(I) catalysts bearing chiral ligands nor chiral counter ion (Table 4.3). In general, most of the reactions did not proceed to give the expected spiro adduct

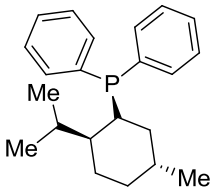
Table 4.3 Optimization of the enantioselective reaction[a]



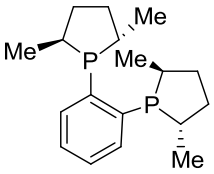
180a **182a**



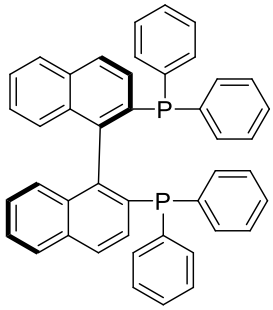
Au_{12}



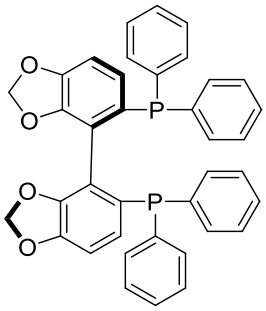
L_1
(S)-Neomanthyl



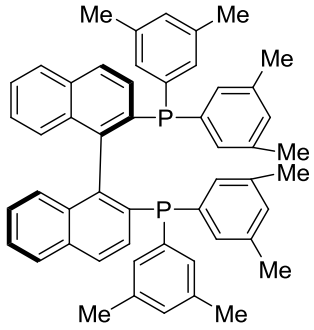
L_2
(S,S)-Me-DUPHOS



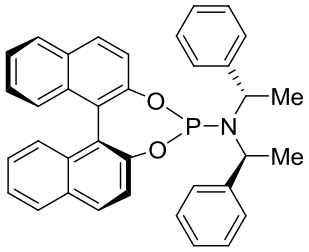
L_3
R-BINAP



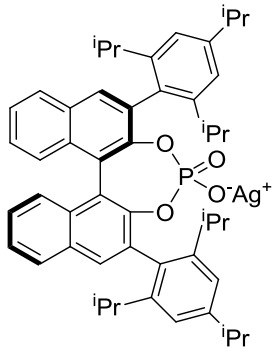
L_4
R-SEGPHOS



L_5
R-DM-BINAP



L_6



Ag-(R)-TRIP

Entry	Temperature (°C)	Catalyst	Solvent	**182a** (%)[b]	**ee** (%)
1	rt	**Au_{12}**	PhMe	-	-
2	rt	**Au_{12}**/ $AgSbF_6$	PhMe	16	7

Table 4.3 *(continued.)*

Entry	Temperature (°C)	Catalyst	Solvent	**182a** (%)[b]	**ee** (%)
3	rt	$AuSMe_2Cl$/**L₁** /$AgSbF_6$	PhMe	-	-
4	rt	$AuSMe_2Cl$/**L₂** /$AgSbF_6$	PhMe	-	-
5	rt	$AuSMe_2Cl$/**L₃** /$AgSbF_6$	PhMe	-[c]	-
6	rt	$AuSMe_2Cl$/**L₄** /$AgSbF_6$	PhMe	-[d]	-
7	rt	PPh_3AuCl/ Ag-(*R*)-TRIP	PhMe	-[e]	-
8	rt	$AuSMe_2Cl$/**L₁** /$AgSbF_6$	CH_2Cl_2	8	0
9[f]	rt	$AuSMe_2Cl$/**L₃** /$AgSbF_6$	CH_2Cl_2	44	0
10[f]	rt	$AuSMe_2Cl$/**L₃** /$AgSbF_6$	CH_2Cl_2/ PhMe	5[g]	0
11[f]	rt	$AuSMe_2Cl$/**L₄** /$AgSbF_6$	CH_2Cl_2/ PhMe	6[g]	0
12[f]	50	$AuSMe_2Cl$/**L₃** /$AgSbF_6$	CH_2Cl_2/ PhMe	25	20
13[h]	50	$AuSMe_2Cl$/**L₃** /$AgSbF_6$	CH_2Cl_2/ Benzene	11	13
14	50	**L₃**Cl/$AgSbF_6$	PhMe	-[i]	-
15	50	**L₃**Cl/ $AgSbF_6$	PhMe	10	5
16	50	$AuSMe_2Cl$/**L₁** /$AgSbF_6$	CH_2Cl_2/ PhMe	-[j]	-
17	50	$AuSMe_2Cl$/**L₂** /$AgSbF_6$	CH_2Cl_2/ PhMe	-[k]	-
18[l]	50	$AuSMe_2Cl$/**L₄** /$AgSbF_6$	CH_2Cl_2/ PhMe	-[m]	-
19[l]	50	$AuSMe_2Cl$/**L₅** /$AgSbF_6$	CH_2Cl_2/ PhMe	28	26
20	50	$AuSMe_2Cl$/**L₆** /$AgSbF_6$	CH_2Cl_2/ PhMe	-	-
21	50	$AuSMe_2Cl$/**L₆** /$AgSbF_6$	CH_2Cl_2/ PhMe	19	23

Table 4.3 *(continued.)*

Entry	Temperature (°C)	Catalyst	Solvent	**182a** (%)[b]	**ee** (%)
22[l]	50	$AuSMe_2Cl$/**L₆** /$AgSbF_6$	CH_2Cl_2/ PhMe	37	22

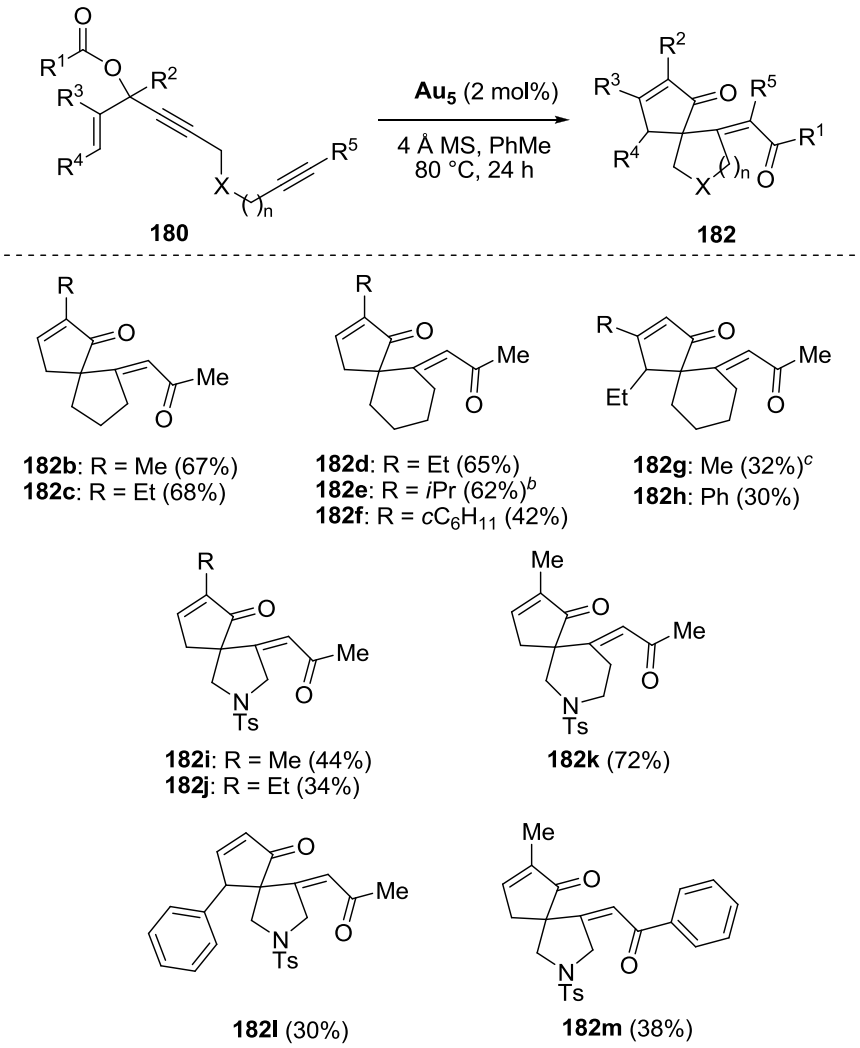
[a] Reactions were carried out in 0.2 mmol scale with 4 Å MS for 24 h. [b] Isolated yield. [c] Starting material recovered in 75% yield. [d] Starting material recovered in 78% yield. [e] Starting material recovered in 70% yield. [f] Reaction was carried out for 84 h [g] ^{1}H NMR yield with dibromomethane (CH_2Br_2) as the internal standard. [h] Reaction was carried out for 72 h. [i] 20% yield of intermediate **181a** obtained. [j] Substrate **180a** and intermediate **181a** were obtained in 25 and 45% yield. [k] Substrate **180a** and intermediate **181a** were obtained in 36 and 23% yield. [l] Reaction was carried out for 48 h. [m] Substrate **180a** and intermediate **181a** were obtained in 65 and 15% yield.

(entries 1, 3-7, 14, 16-18 and 20). When chiral NHC-gold(I) complex catalyst was employed, the spiro compound was obtained in 16% yield with enantiomeric excess (ee) value of 7% (entry 2). Utilizing chiral a counter anion was also found to be ineffective, with 70% of the substrate recovered (entry 7).[94] Changing the solvent from toluene to dichloromethane with **L₁** as the chiral ligand was shown to furnish **182a** in 8% yield, but with no ee value (entry 8). Likewise, the analogous reaction with **L₃** was found to give **182a** in 44% yield with no ee value (entry 9). To increase the ee value via possible π-stacking of the unsaturated systems in both substrate and ligand of the catalyst, a dual solvent system with CH_2Cl_2/PhMe was employed and it was found that **182a** was

obtained in low yields of 5-6% (entry 10-11). When the reaction was repeated at 50 °C, the expected spiro adduct **182a** was obtained in 25% yield with ee value of 20% (entry 12). Further altering the solvent system to CH_2Cl_2/benzene was found to furnish a lower yield of the spirocyclic compound in 11% yield, with lower ee value of 13% (entry 13). Reactions with other ligands, such as $\mathbf{L_5}$ and $\mathbf{L_6}$, were also found to be ineffective in increasing the product yield and ee value, giving the highest yield of 37% and ee value of 26% (entries 15, 19, and 21-22). It is noteworthy that reactions with $\mathbf{L_1}$, $\mathbf{L_2}$ and $\mathbf{L_3}$ were found to furnish the cyclopentadiene intermediate **181a** in 20-45% yields (entries 14, 16-17).

With the optimum conditions in hand, we next sought to define the generality of this methodology with various 1-ene-4,*m*-diyne esters **180b**-**m** to the synthesis of spiro[4.*n*]-ketone **182b**-**m** (Table 4.4). In general, the present procedure was shown to tolerate a variety of 1-ene-4,*m*-diyne esters. Reactions of 1-ene-4,9-diyne ester **180b** and **180c** with 5 mol% of gold(I) phosphine complex $\mathbf{Au_5}$ were found to furnish the corresponding (E)-(2-oxopropylidene)spiro[4.4]non-2-en-1-ones **182b** and **182c** in moderate yields of 67 and 68%, respectively. The analogous reactions with 1-ene-4,10-diyne esters bearing ethyl (**180d**), bulky cyclohexane (**180f**), methyl (**180g**) and phenyl (**180h**) moieties were also shown to be well tolerated, giving the spirocylic adducts in 30-65% yields. The only exception was the reaction of 1-ene-4,10-diyne esters bearing isopropyl (**180e**) has to be carried out in rt to furnish the respective spiro[4.5]-ketone in 62% yield. Similarly, reactions under the same conditions with substrates bearing nitrogen heteroatom were also found to be able to furnish the expected azaspiro compounds. The presence of different substituent such as methyl (**180i**), ethyl (**180j**) and phenyl (**180l** and **180m**) in

Table 4.4 Cycloisomerization of 1-ene-4,*m*-diyne ester **180b-m** catalyzed by $\mathbf{Au_5}$[a]



[a] Unless otherwise stated, all reactions were carried out at the 0.2 mmol scale and 80 mg of 4 Å MS with 5 mol% of $\mathbf{Au_5}$ in toluene at 50 °C for 24 h. Values in parentheses denote isolated product yields. [b] Reaction carried out at rt for 18 h. [c] Reaction carried out for 1.5 h at 0 °C followed by 5.5 h at rt.

the starting 1-ene-4,9-diyne esters furnished the azaspiro [4.4] non-7-en-6-one **182i, 182j**, **182l**, **182m** in low yields of 30-44%. On the other hand, reaction of 1-ene-4,10-diyne esters **180k** furnished the azaspiro[4.5]dec-2-en-1-one in a higher yield of 72%. This could be due to less ring strain in the formation of 6-membered ring as compared to the 5-membered ring.

In the course of our study on substrate scope, it was found that some of the 1-ene-4,*m*-diyne esters were unable to be cycloisomerized under the present reaction procedure as shown in Figure 4.1. In our hands, diyne esters **180n-r** were found to decompose into a mixture of unidentified compounds. ^{1}H NMR analysis of the crude mixture showed no starting material was left and no expected product was observed. On the other hand, 1-ene-4,10-diyne esters **180s** and **180t** was found to be resistant to the reaction condition. In addition, several 1-ene-4,*m*-diynols **185u-β** were unable to be protected to form the

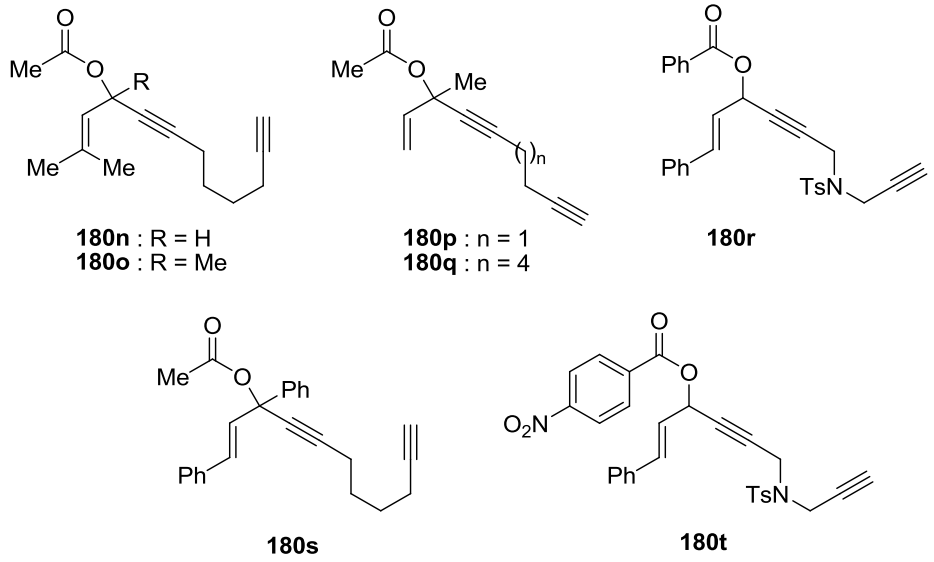


Figure 4.1 1-ene-4,*m*-diyne esters **180n-t**

expected 1-ene-4,*m*-diyne ester (Figure 4.2). In our hands, alcohols **185u-z** were shown to be resistant to he acetylation of the alcohol moiety, resulting in sole recovery of the starting alcohol. This could be due to the steric hinderance of the substituent on the respective substrates. Unexpectedly, competitive 1,3-migration of the acyloxy moiety to

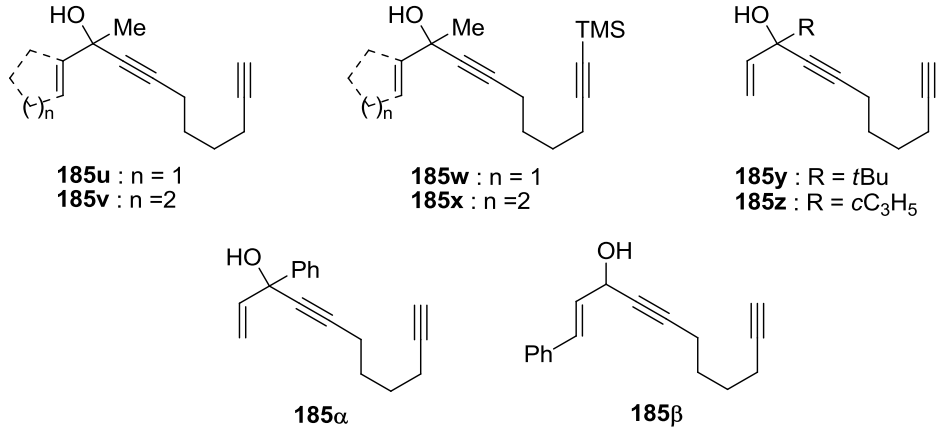
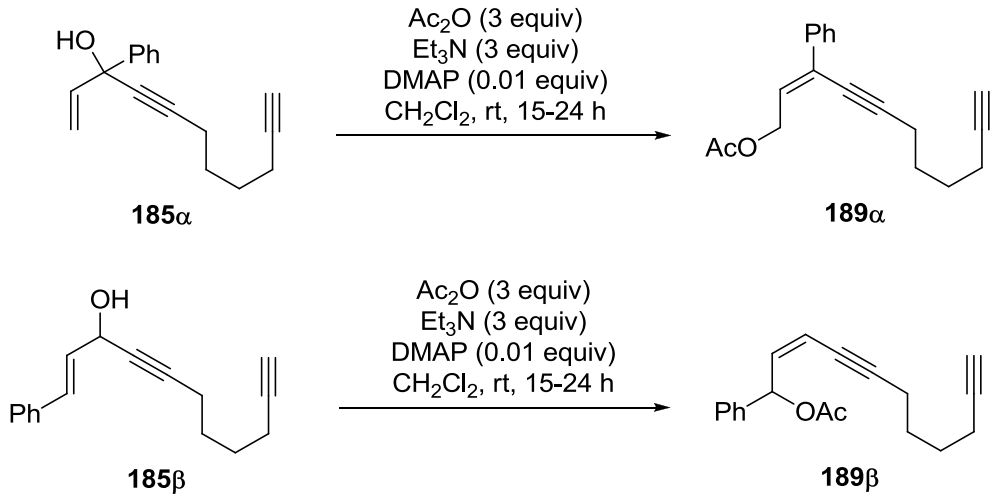


Figure 4.2 1-ene-4,*m*-diynols **185u-β**

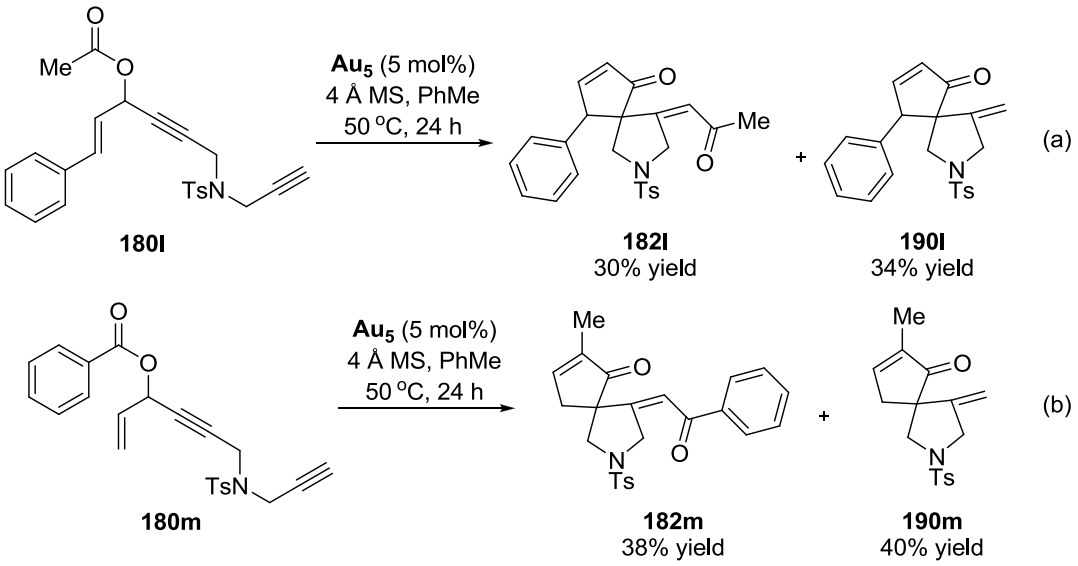


Scheme 4.4 1,3-migration of the acyloxy moiety to the alkene unit in the protection of 1-ene-4,10-diynols **185α** and **185β**

the alkene unit was observed for alcohols **185α-β**, furnishing the corresponding esters **189α-β** quantitatively (Scheme 4.4).

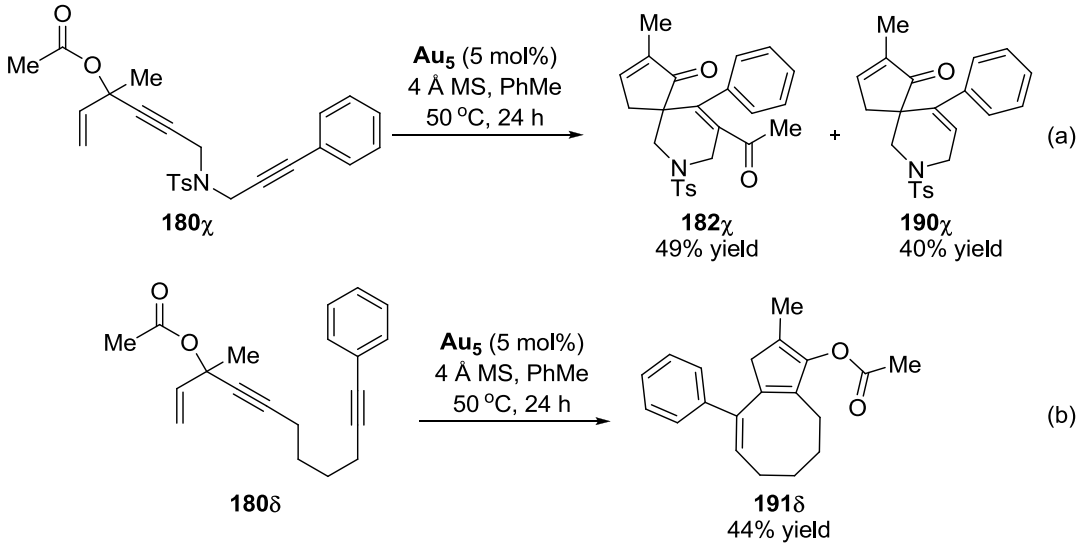
The reaction of 1-ene-4,9-diyne esters containing a nitrogen heteroatom, **180l** and **180m**, in the presence of gold(I) phosphine complex $\mathbf{Au_5}$ in the optimum condition were observed to furnish the azaspiro compounds **190l** and **190m** in slightly higher yields of 34 and 40% than the expected spiro[4.4]-ketone as mentioned in Table 4.4 (Scheme 4.5). The formation of **190** might be due to the competitive hydrolysis pathway present in this series of substrates. While not listed, an attempt to control the selectivity by increasing the amount of 4 Å MS in the reaction was shown to have no effect on the course of the reaction, giving both of the azaspiro compounds **182l-m** and **190l-m** in similar yields.

A different reactivity pattern was observed when substrates bearing phenyl moiety on

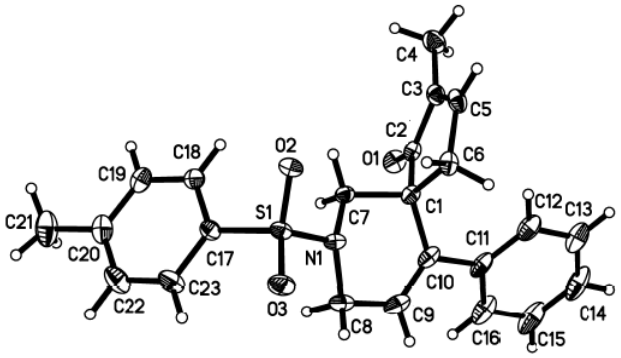


Scheme 4.5 Reactions of **180l** and **180m** in the presence of $\mathbf{Au_5}$ to give **182l-m** and **190l-m**

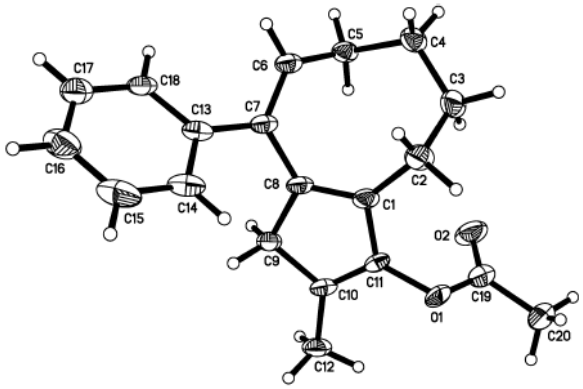
the distal alkyne unit were subjected to the present methodology. In the presence of gold(I) phosphine complex catalyst **Au_5** and 4 Å MS in toluene for 24 h, 1-ene-4,6-diyne ester **180χ** was found to furnish the spiro[4.5]-ketone adduct **182χ** and azaspiro compound **190χ** in 39 and 40% yield, respectively (Scheme 4.6, eq. a). This finding suggested that a 6-*endo*-*dig* cyclization has occurred in place of the 5-*exo*-*dig* cyclization observed for other nitrogen containing substrates bearing a terminal alkyne group.[95] On the other hand, 1-ene-4,6-diyne ester **180δ** was shown to give (*Z*)-2-methyl-9-phenyl-4,5,6,7-tetrahydro-1H-cyclopenta[8]annulen-3-yl acetate **191δ** in 44% yield (Scheme 4.6, eq. b). The structure of the azaspiro compound **190χ** and the fused ring adduct **191δ** was confirmed by both ^{1}H,^{13}C NMR analysis and X-ray structure crystallography[96] as depicted in Figure 4.3.



Scheme 4.6 Reactions of **180χ** and **180δ** in the presence of **Au_5**



(a) **190χ**

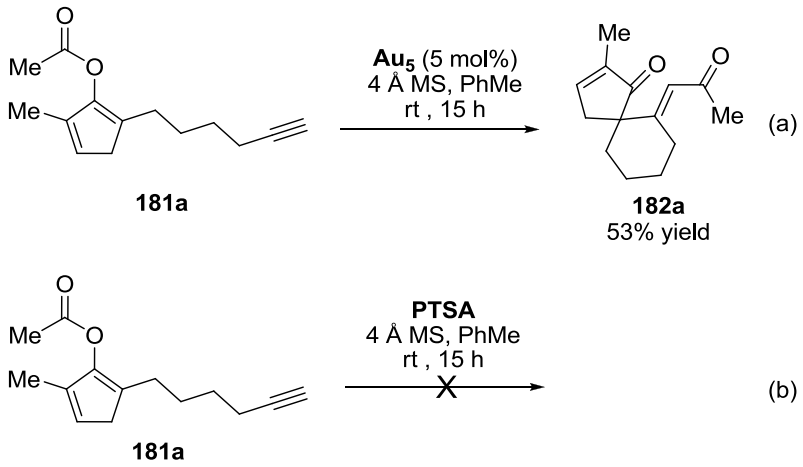


(b) **191δ**

Figure 4.3 ORTEP drawing of azaspiro compound **190χ** (a) and (*Z*)-2-methyl-9-phenyl-4,5,6,7-tetrahydro-1H-cyclopenta[8]annulen-3-yl acetate **191δ** (b) with thermal ellipsoids at 50% probability levels

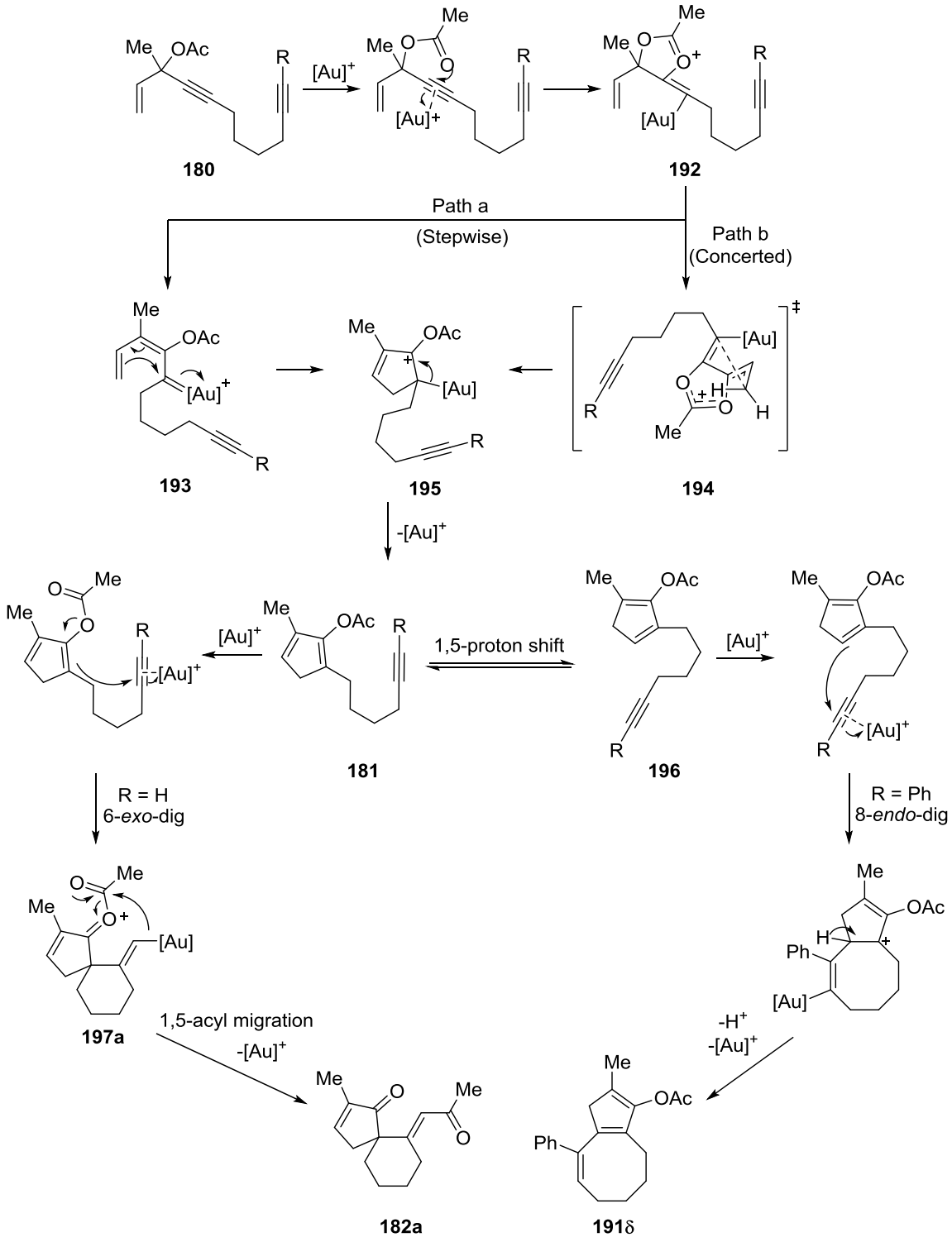
Next, we sought to study the mechanistic premise put forward in Scheme 4.1. As depicted earlier in Table 4.2, the isolation of the cyclopentadiene adduct **181a** under certain condition suggested its involvement in the reaction. This hypothesis was corroborated by a control reaction utilizing cyclopentadiene adduct **181a**. In the presence of gold(I) phosphine complex $\mathbf{Au_5}$ in toluene at room temperature for 15 h, the expected spiro[4.5]-ketone product **182a** was obtained in 53% yield (Scheme 4.7, eq a). It is

noteworthy that the cyclopentadiene adduct is a highly reactive substrate which would decompose in a short period of time. Another control experiment was carried out to define the role of gold(I) phosphine complex **Au_5** in the reaction (Scheme 4.7, eq b). It was found that altering the Lewis acidic catalyst to Brønsted acid *p*-toluenesulfonic acid (PTSA) led to decomposition of the starting material, further confirming the importance of the gold(I) metal complex as a catalyst.



Scheme 4.7 Control experiments with **181a** in the presence of gold(I) phosphine catalyst **Au_5** (a) and in the presence of PTSA as an acid (b)

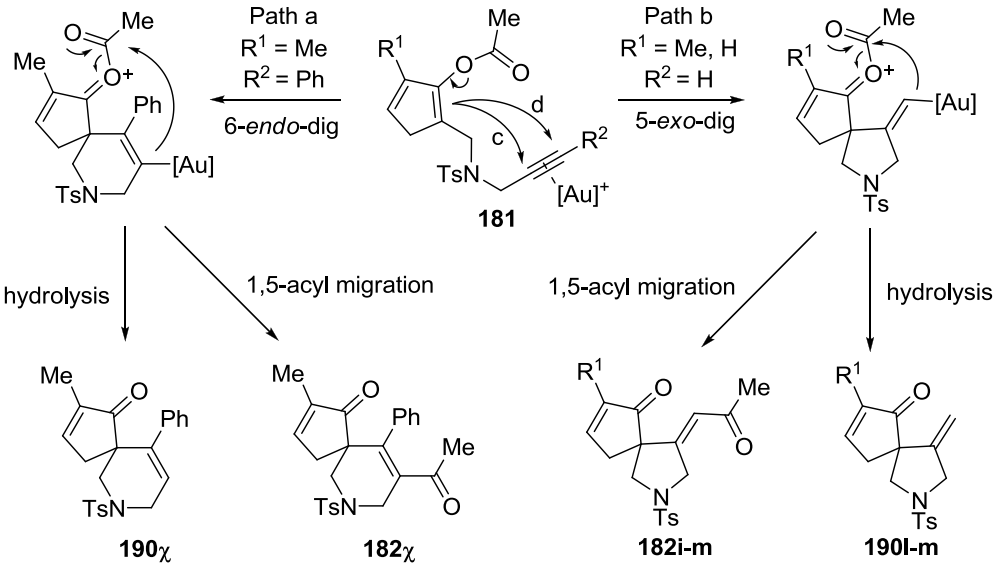
On the basis of the results obtained, plausible mechanisms for the transformation were proposed (Scheme 4.8 and 4.9). As depicted in Scheme 4.8, the formation of the carbocycles was thought to be initiated by an initial [2,3]-sigmatropic rearrangement of the ester moiety to the 1,3-dioxin-1-ium intermediate **192**. A subsequent metallo-Nazarov type cyclization was then proposed to take place either in a stepwise (Scheme 4.8, path a) or concerted manner[33] (Scheme 4.8, path b), to generate the cyclopentadiene intermediate



Scheme 4.8 Proposed mechanism for the cycloisomerization of **180a-h** and **180δ** catalyzed by gold(I) phosphine complex $\mathbf{Au_5}$

181 after deauration of the putative intermediate **195**. Depending on the substitution pattern on the distal alkyne tether, two divergent reaction pathway then took place. In the case whereby R = H, activation of the alkyne moiety of the cyclopentadiene intermediate **181** triggered a 6-*exo*-*dig* cyclization to give the gold carbenoid intermediate **197a**, which underwent a rapid 1,5-acyloxy migration to furnish the corresponding spiro[4.5]-ketone product. On the other hand, substrate with R = Ph was thought to first undergo a 1,5-proton shift before the activation of the alkyne moiety. An 8-*endo*-*dig* cyclization and protodeauration then took place to furnish the 5,8-fused ring adduct **191δ**.

For substrates containing nitrogen heteroatom, the intermediate was thought to undergo two different pathways, also depending on the substituent pattern on the distal alkyne group (Scheme 4.8). When R^2 = Ph, 6-*endo*-*dig* cyclization was thought to take



Scheme 4.8 Proposed mechanism for the cycloisomerization of **180i-m** and **180χ** catalyzed by gold(I) phosphine complex **Au_5**

place as depicted in Scheme 4.8, path a. On the other hand, substrates with R^2 = H underwent 5-*exo*-*dig* cyclization (Scheme 4.8, path b). A competitive hydrolysis and 1,5-acyl migration pathways could then take place to give two different azaspiro products.

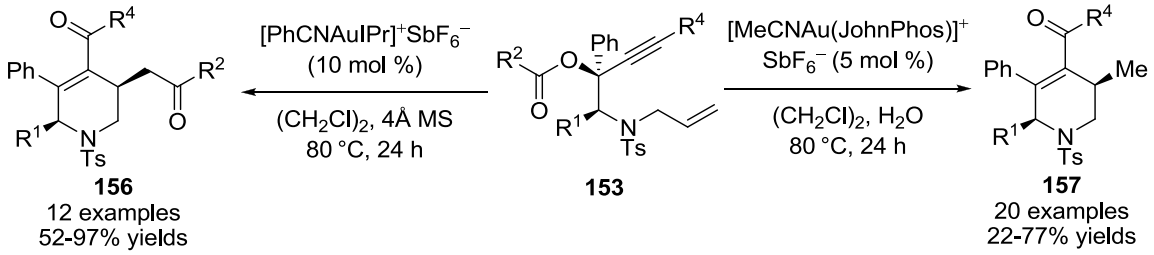
4.3 Conclusion

In summary, we have demonstrated an efficient and elegant gold(I) catalyzed synthetic route via cycloisomerization of 1-ene-4,*m*-diyne esters to prepare various cyclic compounds. This methodology was shown to be able to access a range of spirocyclic compounds in a single step from readily accessible 1-ene-4,*m*-diyne ester. Although the scope of the reaction is limited, this methodology is notable as one step formation of spirocyclic substrate from an acyclic precursor via further transformation of the cyclopentadiene moiety furnished from the well reported [2,3]-sigmatropic rearrangement/ Nazarov cyclization has not been observed before.

Chapter V. Concluding Remarks

Gold as a Lewis acidic transition metal catalyst was shown to be a powerful and effective catalyst in the synthesis of cyclic compounds. In this work, three gold-catalyzed intramolecular based approaches for the synthesis of *cis*-1,2,3,6-tetrahydropyridin-4-yl ketones, *cis*-cyclohepta-4,8-diene-fused pyrrolidines and spiro[4.*n*]-ketones from unsaturated precursors were described.

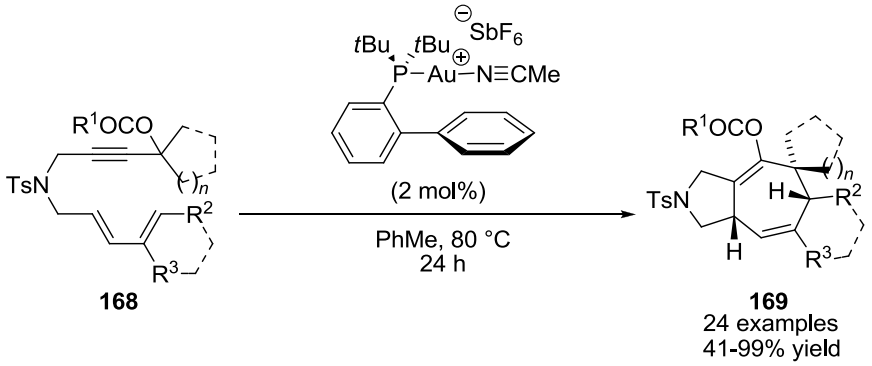
An efficient methodology to obtain a variety of *cis*-1,2,3,6-tetrahydropyridin-4-yl ketones **157** and δ-diketones **156** from 1,7-enyne esters **153** was presented in Chapter II (Scheme 5.1). This study revealed that the difference in the steric and electronic properties of the gold(I) phosphine and NHC-gold(I) complex catalysts were able to control product selectivity via the difference in rate of protodeauration of the gold(I) complexes in one of the intermediate. This protocol was also shown to be applicable to a wide range of 1,7-enyne esters, including substrates bearing heteroatom such as oxygen and sulfur. Furthermore, the reaction was found to proceed with complete conversion of



Scheme 5.1 Cycloisomerization of 1,7-enyne esters **153** to *cis*-1,2,3,6-tetrahydropyridin-4-yl ketones **157** and δ-diketones **156**

the chirality from the substrate to product via steric control of the gold(I) complex catalyst with the intermediate. DFT analysis of the intermediate eluded the possibility of thermodynamic control of the reaction. The application of this present methodology was exemplified in the formation of stereochemically well-defined bioactive 2,3,4,4*a*,5,9*b*-hexahydroindeno[1,2-*c*]pyridine family of compounds in two steps with an excellent overall yield from one of the adduct obtained.

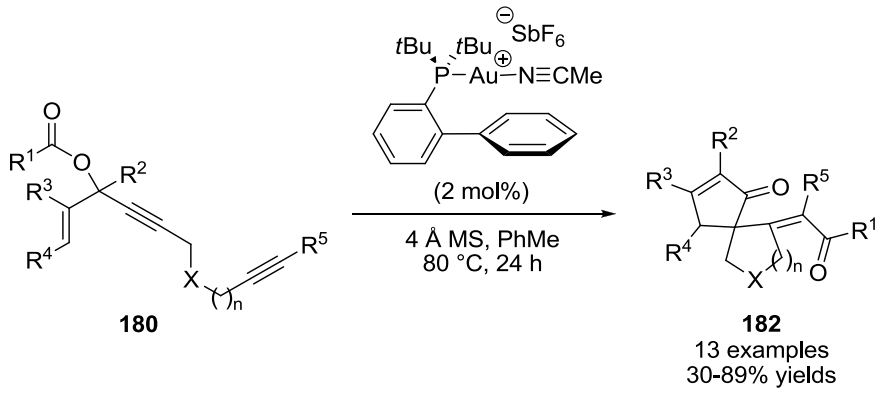
In Chapter III, a synthetic method involving cycloisomerization of 1,6,8-dienyne carbonates and esters **168** in the presence of gold(I) phosphine catalyst $[MeCNAu(JohnPhos)]^{+}SbF_6^{-}$ for the synthesis of *cis*-cyclohepta-4,8-diene-fused pyrrolidines **169** was reported (Scheme 5.2). The scope of this methodology was shown to include substrates bearing multiple rings, spirocyclic moiety and heteroatom. This study is mechanistically interesting as it serves as an evidence for the reversibility of [2,3]- and [3,3]- sigmatropic rearrangement via ^{18}O-labelling experiment. In addition, the suggested reaction pathways provide an unique instance in this field of homogenous



Scheme 5.2 Cycloisomerization of 1,6,8-dienyne carbonates and esters **168** to *cis*-cyclohepta-4,8-diene-fused pyrrolidines **169**

gold catalysis where the initial [2,3]- or [3,3]-sigmatropic rearrangement did not influence product selectivity.

Gold catalyzed cycloisomerization of unsaturated precursor bearing an alkene and two alkyne units, 1-ene-4,*m*-diyne esters **180**, to the synthesis of spiroketones **182** was delineated in Chapter IV (Scheme 5.3). This methodology was shown to provide the spirocyclic compounds in moderate to good yields of 30-89%. The mechanism was proposed to involve an initial [2,3]-sigmatropic rearrangement followed by metallo-Nazarov cyclization to form the cyclopentadiene intermediate, which in the presence of gold(I) phosphine catalyst was reasoned to undergo a second cyclization involving the pendant alkyne moiety in the intermediate to form the spiroketone. In addition, this synthetic pathway was shown to be potentially useful in the synthesis of other types of cyclic compounds.



Scheme 5.3 Cycloisomerization of 1-ene-4,*m*-diyne esters **180** to spiroketones **182**

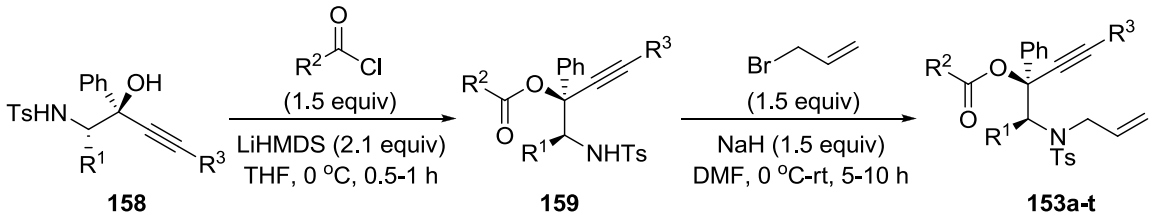
Chapter VI. Experimental Section

6.1 General Remarks

Unless specified, all reagents and starting materials were purchased from commercial sources and used as received. Solvents were purified following standard literature procedures. Analytical thin layer chromatography (TLC) was performed using Merck 60 F254 pre-coated silica gel plate. Visualization was achieved by UV light (254 nm). Flash chromatography was performed using Merck silica gel and gradient solvent system. 1H spectra were measured on 300, 400 and 500 MHz spectrometers. Chemical shifts (ppm) were recorded with respect to TMS in CDCl3. Multiplicities are given as: s (singlet), brs (broad singlet), d (doublet), t (triplet), q (quartet), qn (quintet), m (multiplet), dd (doublet of doublets), dt (doublet of triplets), qd(quartet of doublets), dqn (doublet of quintets) or td (triplet of doublets). The number of protons (*n*) for a given resonance is indicated by *n*H. Coupling constants are reported as *J* values in Hz. Infrared spectra were recorded on Shimadzu IR Prestige-21 FTIR Spectrometer. High resolution mass spectra (HRMS) were obtained using a LC/HRMS TOF spectrometer using simultaneous electrospray (ESI). Mass spectral data are reported in units of mass to charge (*m*/*z*). Optical rotations were measured in $CHCl_3$ on a polarimeter with a sodium vapor lamp at 589 nm and 10 cm cell (*c* given in g/100 mL).

6.2 Gold Catalyzed Cycloisomerization of 1,7-Enyne Esters to Structurally Diverse *cis*-1,2,3,6-Tetrahydropyridin-4-yl Ketone

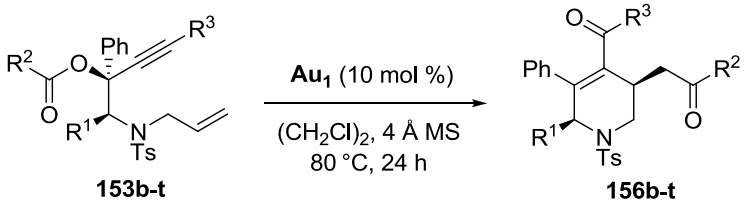
General Procedure for the Preparation of 1,7-Enyne Esters 153a-t



To a solution of the appropriate *N*-allyl-*N*-((3*S*,4*S*)-3-hydroxy-1,3,5-substituted-alk-4-yn-2-yl)-4-methylbenzenesulfonamide **158**[48,57] (1 mmol) in THF (5 mL) was added LiHMDS (2.1 mL, 2.1 mmol, 1.0 M in THF) at 0 °C. The reaction solution was stirred at this temperature for another 20 min. The appropriate acyl chloride (1.5 mmol) was then added and stirred at the same temperature for 30 min. Upon completion indicated by TLC, the reaction mixture was quenched with saturated NH_4Cl solution (10 mL) and the organic layer was extracted with EtOAc (3 x 15 mL). The combined organic layers were then washed with brine (10 mL), dried over $MgSO_4$, concentrated under reduced pressure and purified by flash column chromatography on silica gel with *n*hexane:EtOAc = 7:1→4:1 as eluent to yield the intermediate **159**. To a solution of the intermediate **159** in DMF (5 mL) was added NaH (60% dispersion in mineral oil, 1.5 eq) followed by allyl bromide (1.5 eq) at 0 °C. The reaction solution was left to warm up to room temperature and stirred for another 5-10 h. Upon completion indicated by TLC, the reaction mixture was quenched with H_2O (10 mL) and the organic layer was extracted with EtOAc (3 x 10 mL). The combined organic layers were then washed with brine (10 mL), dried over $MgSO_4$, concentrated under reduced pressure and purified by flash column

chromatography on silica gel with *n*Hex:EtOAc = 9:1→ 6:1 as eluent to give the title compound.

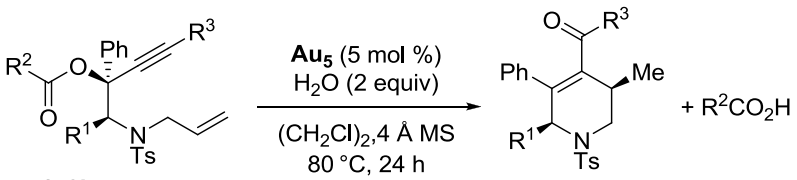
General Experimental Procedure for NHC-gold(I) Complex Au_1-Catalyzed Cycloisomerization of 1,7-Enyne Esters 153 to *cis*-1,2,3,6-Tetrahydropyridin-4-yl δ-Diketone Derivatives 156



153b-t **156b-t**

To a solution of the 1,7-enyne ester **153** (0.2 mmol) and 4Å MS (100 mg) in 1,2-dichloroethane (2 mL) was added gold(I) complex **Au_1** (20 μmol). The reaction mixture was stirred at 80 °C for 24 h. The reaction mixture was then cooled to room temperature, filtered through Celite, washed with CH_2Cl_2 and concentrated under reduced pressure. Purification by flash column chromatography on silica gel with *n*Hex/EtOAc = 7:1→to 3:1 as eluent gave the title compound.

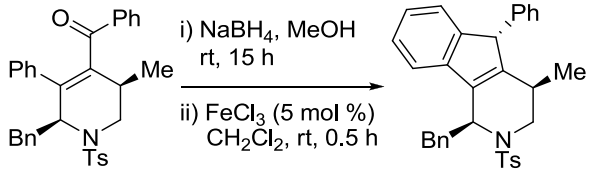
General Experimental Procedure for Au(I) Complex Au_5-Catalyzed Cycloisomerization of 1,7-Enyne Esters 153 to *cis*-1,2,3,6-Tetrahydropyridin-4-yl Ketone Derivatives 157



153b-g, m, p, s **157b-g, m, p, s**

To a solution of 1,7-enyne ester **153** (0.2 mmol) and H_2O (0.4 mmol) in 1,2-dichloroethane (2 mL) was added gold(I) complex **Au_5** (10 μmol). The reaction mixture was stirred at 80 °C for 24 h. The reaction mixture was then cooled to room temperature and the solvent was removed under reduced pressure. Purification by flash column chromatography on silica gel (*n*Hex/EtOAc = 9:1→6;1 as eluent) gave the title compound.

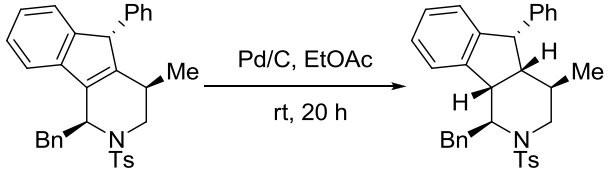
Experimental Procedure for the Preparation of (1*S*,4*R*,5*S*)-1-Benzyl-4-methyl-5-phenyl-2-tosyl-2,3,4,5-tetrahydro-1*H*-indeno[1,2-*c*]pyridine (166)



157a **166**

To a solution of **157a** (0.3 mmol) in MeOH (3 mL) in room temperature, $NaBH_4$ (9 mmol) was added and the reaction mixture was left to stir for 15 h. Upon completion, the reaction mixture was quenched with H_2O (10 mL) and extracted with EtOAc (3 x10 mL). The combined organic layers were washed with brine (20 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The crude residue was dissolved in CH_2Cl_2 (3 mL) and anhydrous $FeCl_3$ (15 μmol) was added. The reaction mixture was stirred at room temperature for 30 min. Removal of the solvent under reduced pressure and purification by flash column chromatography on silica gel with *n*Hex/EtOAc = 9:1 as eluent gave the title compound in 94% yield.

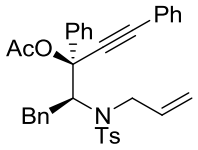
Experimental Procedure for the Preparation of (1*S*,4*R*,4*aR*,5*S*,9*bS*)-1-Benzyl-4-methyl-5-phenyl-2-tosyl-2,3,4,4*a*,5,9*b*-hexahydro-1*H*-indeno[1,2-*c*]pyridine (167)



166 **167**

To a solution of **166** (0.2 mmol) in EtOAc (5 mL), 10% of Pd/C (22 mg) was added under a H_2 gas atmosphere. The reaction mixture was stirred at room temperature for 20 h. The reaction mixture was then filtered through Celite, washed with EtOAc (20 mL) and concentrated under reduced pressure. Purification by flash column chromatography on silica gel with *n*Hex/EtOAc = 9:1 as eluent gave the title compound in 91% yield.

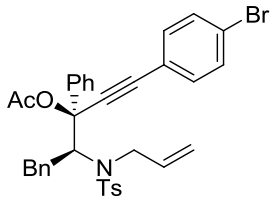
(3*S*,4*S*)-4-(*N*-Allyl-4-methylphenylsulfonamido)-1,3,5-triphenylpent-1-yn-3-yl Acetate (153a)



Yield 75%, 0.423 g; colourless solid, m.p. = 185-186 °C; $[\alpha]_D^{23}$ −4.5 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.04 (s, 3H), 2.27 (s, 3H), 3.08 (dd, 1H, *J* = 14.5, 9.6 Hz), 3.37 (dd, 1H, *J* = 14.7, 3.9 Hz), 4.02 (dd, 1H, *J* = 16.8, 7.2 Hz), 4.12 (dd, 1H, *J* = 16.8, 7.2 Hz), 4.91 (d, 1H, *J* = 10.2 Hz), 5.01 (d, 1H, *J* = 17.3 Hz), 5.17 (d, 1H, *J* = 5.8 Hz), 5.61-5.63 (m, 1H), 6.79 (d, 2H, *J* = 7.8 Hz), 6.85 (d, 2H, *J* = 8.2 Hz), 7.11-7.24 (m, 5H), 7.31-7.43 (m, 6H), 7.60-7.63 (m, 2H), 7.67 (d, 1H, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.4, 21.8, 34.7, 46.9, 68.6, 82.5, 86.4, 90.8, 116.3, 122.2, 126.5, 126.5, 127.9, 128.3, 128.4, 128.6, 129.0, 129.0, 129.6, 132.2, 136.1, 137.3, 138.6, 139.2, 142.5, 167.5;

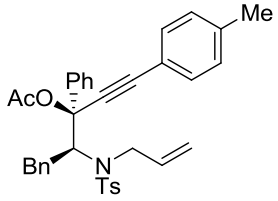
IR (NaCl, neat) *v*: 3019, 2232, 1755, 1215 cm^{-1}; HRMS (ESI) calcd. for $C_{35}H_{33}NO_4SNa$ (M++Na): 586.2028, found: 586.2035.

(3*S*,4*S*)-4-(*N*-Allyl-4-methylphenylsulfonamido)-1-(4-bromophenyl)-3,5-diphenylpent-1-yn-3-yl Acetate (153b)



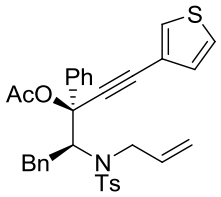
Yield 72%, 0.463 g; colourless solid, m.p. = 181-183 °C; $[\alpha]_D^{23}$ +8.3 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): δ 2.14 (s, 3H), 2.29 (s, 3H), 3.03 (dd, 1H, *J* = 14.5, 10.2 Hz), 3.25 (dd, 1H, *J* = 14.7, 3.0 Hz), 4.00 (dd, 1H, *J* = 16.9, 6.9 Hz), 4.21 (dd, 1H, *J* = 16.9, 4.5 Hz), 4.98 (d, 1H, *J* = 10.2 Hz), 5.08 (d, 1H, *J* = 17.3 Hz), 5.15 (dd, 1H, *J* = 9.6, 2.8 Hz), 5.69-5.78 (m, 1H), 6.81 (d, 2H, *J* = 8.1 Hz), 6.87 (d, 2H, *J* = 8.1 Hz), 7.01 (d, 2H, *J* = 6.7 Hz), 7.19-7.25 (m, 3H), 7.37-7.49 (m, 5H), 7.53 (d, 2H, *J* = 8.6 Hz), 7.65 (d, 2H, *J* = 7.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.5, 21.8, 33.7, 46.9, 69.4, 82.8, 87.8, 89.4, 116.2, 121.3, 123.3, 126.3, 126.5, 127.7, 128.4, 128.5, 128.7, 129.0, 129.4, 131.6, 133.7, 136.3, 137.2, 138.4, 139.1, 142.4, 167.6; IR (NaCl, neat) *v*: 3447, 3019, 2234, 1753, 1215 cm^{-1}; HRMS (ESI) calcd. for $C_{35}H_{32}NO_4S^{79}BrNa$ (M^++Na): 664.1133, found: 664.1140.

(3*S*,4*S*)-4-(*N*-Allyl-4-methylphenylsulfonamido)-3,5-diphenyl-1-(*p*-tolyl)pent-1-yn-3-yl Acetate (153c)



Yield 73%; 0.422 g; colourless solid, m.p. = 153-154 °C; $[\alpha]_D^{23}$ −2.3 (*c* 1.0, CHCl3); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.02 (s, 3H), 2.28 (s, 3H), 2.35 (s, 3H), 3.09 (dd, 1H, *J* = 14.4, 9.5 Hz), 3.40 (dd, 1H, *J* = 14.6, 4.1 Hz), 4.02 (dd, 1H, *J* = 16.7, 7.2 Hz), 4.13 (dd, 1H, *J* = 14.0, 6.9 Hz), 4.90 (d, 1H, *J* = 10.2 Hz), 5.00 (d, 1H, *J* = 17.2 Hz), 5.17-5.18 (m, 1H), 5.54-5.60 (m, 1H), 6.78 (d, 1H, *J* = 7.9 Hz), 6.86 (d, 2H, *J* = 8.2 Hz), 7.13-7.15 (m, 4H), 7.23-7.25 (m, 3H), 7.34-7.43 (m, 3H), 7.50 (d, 2H, *J* = 8.0 Hz), 7.67 (d, 2H, *J* = 7.3 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.4, 21.6, 21.8, 34.9, 46.9, 68.5, 82.5, 85.8, 91.1, 116.4, 119.1, 126.5, 126.6, 127.9, 128.3, 128.4, 128.6, 129.0, 129.1, 129.6, 132.1, 136.1, 137.4, 138.7, 139.2, 139.3, 142.5, 167.5; IR (NaCl, neat) *v*: 3019, 2232, 1753, 1215 cm^{-1}; HRMS (ESI) calcd. for $C_{36}H_{35}NO_4SNa$ (M^++Na): 600.2185, found: 600.2186.

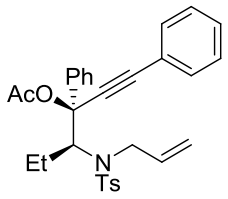
(3*S*,4*S*)-4-(*N*-Allyl-4-methylphenylsulfonamido)-3,5-diphenyl-1-(thiophen-3-yl)pent-1-yn-3-yl Acetate (153d)



Yield 82%; 0.467 g; colourless solid, m.p. = 192-194 °C; $[\alpha]_D^{23}$ +1.9 (*c* 0.4, $CHCl_3$); ^{1}H

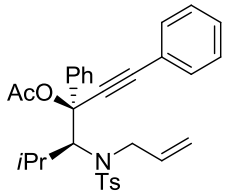
NMR ($CDCl_3$, 400 MHz): δ 2.07 (s, 3H), 2.28 (s, 3H), 3.03 (dd, 1H, J = 14.2, 10.0 Hz), 3.29 (dd, 1H, J = 14.7, 3.4 Hz), 4.00 (dd, 1H, J = 16.8, 7.0 Hz), 4.15 (d, 1H, J = 16.5 Hz), 4.94 (d, 1H, J = 10.2 Hz), 5.04 (d, 1H, J = 17.3 Hz), 5.13 (d, 1H, J = 7.4 Hz), 5.67-5.68 (m, 1H), 6.78-6.87 (m, 4H), 7.04-7.29 (m, 7H), 7.33-7.43 (m, 3H), 7.63-7.70 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.4, 21.8, 34.2, 46.9, 69.0, 82.8, 86.0, 86.1, 116.2, 121.3, 125.2, 126.4, 126.5, 127.8, 128.3, 128.5, 128.6, 129.0, 129.5, 130.3, 130.5, 136.3, 137.3, 138.6, 139.2, 142.4, 167.6; IR (NaCl, neat) v: 3026, 2232, 1755, 1217 cm^{-1}; HRMS (ESI) calcd. for $C_{33}H_{31}NO_4S_2Na$ (M^++Na): 592.1592, found: 592.1595.

(3*S*,4*S*)-4-(*N*-Allyl-4-methylphenylsulfonamido)-1,3-diphenylhex-1-yn-3-yl Acetate (153e)



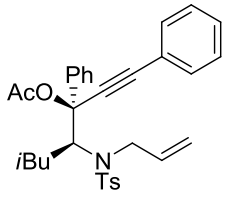
Yield 66%; 0.397 g; colourless solid, m.p. = 141-142 °C; $[\alpha]_D^{23}$ −34.0 (c 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.88 (t, 3H, J = 7.4 Hz), 1.92-2.05 (m, 2H), 2.12 (s, 3H), 2.32 (s, 3H), 4.01-4.05 (m, 2H), 4.65 (dd, 1H, J = 9.8, 3.1 Hz), 4.89-5.00 (m, 1H), 5.04 (d, 2H, J = 1.2 Hz), 5.72-5.82 (m, 1H), 7.04 (d, 2H, J = 8.1 Hz), 7.21 (d, 2H, J = 8.0 Hz), 7.29-7.43 (m, 6H), 7.52-7.64 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 11.7, 20.6, 21.5, 22.0, 46.7, 68.0, 82.2, 86.6, 90.2, 116.3, 122.2, 126.5, 128.1, 128.2, 128.3, 128.4, 128.8, 129.1, 132.0, 135.9, 137.4, 139.7, 142.9, 167.6; IR (NaCl, neat) v: 3018, 2232, 1753, 1217 cm^{-1}; HRMS (ESI) calcd. for $C_{30}H_{31}NO_4SNa$ (M^++Na): 524.1872, found: 524.1877.

(3*S*,4*S*)-4-(*N*-Allyl-4-methylphenylsulfonamido)-5-methyl-1,3-diphenylhex-1-yn-3-yl Acetate (153f)



Yield 70%; 0.361 g; colourless solid, m.p. = 147-149 °C; $[\alpha]_D^{23}$ −32.1 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): δ 1.08 (d, 3H, *J* = 6.7 Hz), 1.24 (d, 3H, *J* = 6.6 Hz), 2.06 (s, 3H), 2.33 (s, 4H), 2.48-2.58 (m, 1H), 3.90 (dd, 1H, *J* = 16.8, 5.1 Hz), 4.19 (dd, 1H, *J* = 16.8, 7.6 Hz), 4.61 (d, 1H, *J* = 9.3 Hz), 4.85 (dd, 1H, *J* = 10.1, 0.9 Hz), 4.97 (dd, 1H, *J* = 17.2, 1.2 Hz), 5.56-5.66 (m, 1H), 7.03 (d, 2H, *J* = 8.2 Hz), 7.16 (d, 2H, *J* = 8.2 Hz), 7.31-7.39 (m, 6H), 7.48-7.51 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.4, 22.0, 22.1, 22.6, 30.4, 47.7, 71.2, 81.8, 86.3, 91.3, 116.7, 122.1, 126.8, 128.2, 128.3, 128.4, 128.4, 128.9, 129.0, 131.8, 135.4, 137.2, 140.1, 142.8, 167.2; IR (NaCl, neat) *v*: 2230, 1755, 1217 cm^{-1}; HRMS (ESI) calcd. for $C_{31}H_{33}NO_4SNa$ (M^++Na): 538.2028, found: 538.2029.

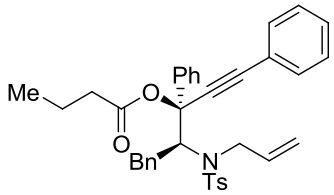
(3*S*,4*S*)-4-(*N*-Allyl-4-methylphenylsulfonamido)-6-methyl-1,3-diphenylhept-1-yn-3-yl Acetate (153g)



Yield 79%; 0.418 g; colourless solid, m.p. = 169-170 °C; $[\alpha]_D^{23}$ −38.1 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): δ 0.91-0.95 (m, 6H), 1.63-1.71 (m, 2H), 1.92-1.98 (t, 3H), 2.13 (s, 3H), 2.33 (s, 3H), 3.91-4.04 (m,2H), 4.86 (d, 2H, *J* = 10.3 Hz), 4.95 (d, 1H, *J* = 17.2

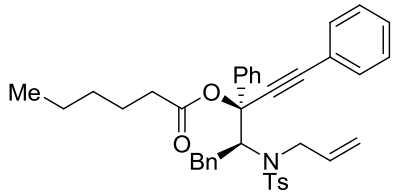
Hz), 5.57-5.67 (m, 1H), 7.04 (d, 2H, *J* = 8.1 Hz), 7.16 (d, 2H, *J* = 8.0 Hz), 7.32-7.42 (m, 6H), 7.51-7.53 (m, 2H); 7.63 (d, 2H, *J* = 6.7 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.5, 21.9, 23.6, 24.1, 37.2, 46.8, 64.1, 82.1, 86.6, 90.3, 116.3, 122.2, 126.6, 128.2, 128.3, 128.4, 129.0, 132.0, 135.9, 137.3, 139.6, 143.0, 167.6; IR (NaCl, neat) *v*: 2957, 2232, 1757, 1219 cm^{-1}; HRMS (ESI) calcd. for $C_{32}H_{35}NO_4SNa$ (M^++Na): 552.2185, found: 552.2185.

(3*S*,4*S*)-4-(*N*-Allyl-4-methylphenylsulfonamido)-1,3,5-triphenylpent-1-yn-3-yl Butyrate (153h)



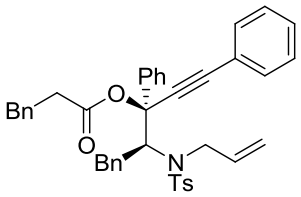
Yield 70%, 0.414 g; colourless solid, m.p. = 88-90 °C; $[\alpha]_D^{23}$ −14.1 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.94 (t, 3H, *J* = 7.4 Hz), 1.57-1.69 (m, 2H), 2.26-2.29 (m, 5H), 3.10 (dd, 1H, *J* = 14.2, 9.8 Hz), 3.41 (dd, 1H, *J* = 14.7, 3.6 Hz), 4.05 (dd, 1H, *J* = 14.7, 7.2 Hz), 4.15 (d, 1H, *J* = 14.2 Hz), 4.90 (d, 1H, *J* = 10.2 Hz), 5.00 (d, 1H, *J* = 17.2 Hz), 5.20 (d, 1H, *J* = 6.4 Hz), 5.56-5.58 (m, 1H), 6.76 (d, 2H, *J* = 7.7 Hz), 6.84 (d, 2H, *J* = 8.0 Hz), 7.14-7.25 (m, 5H), 7.33-7.43 (m, 6H), 7.59-7.61 (m, 2H), 7.68 (d, 2H, *J* = 7.4 Hz); ^{13}C NMR (CDCl3, 100 MHz): δ 13.7, 18.4, 21.4, 34.9, 36.8, 46.9, 68.6, 82.2, 86.5, 90.7, 116.4, 122.3, 126.5, 126.6, 127.9, 128.3, 128.4, 128.4, 128.6, 128.9, 129.0, 129.6, 132.1, 136.0, 137.4, 138.7, 139.3, 142.5, 170.1; IR (NaCl, neat) *v*: 3318, 2235, 1749, 1215 cm^{-1}; HRMS (ESI) calcd. for $C_{37}H_{37}NO_4SNa$ (M^++Na): 614.2341, found: 614.2356.

(3*S*,4*S*)-4-(*N*-Allyl-4-methylphenylsulfonamido)-1,3,5-triphenylpent-1-yn-3-yl Hexanoate (153i)



Yield 70%; 0.434 g, yellow oil; $[\alpha]_D^{23}$ −12.5 (*c* 1.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.88 (t, 3H, *J* = 6.5 Hz), 1.30-1.32 (m, 4H), 1.56-1.63 (m, 2H), 2.26-2.30 (m, 5H), 3.11 (dd, 1H, *J* = 14.2, 9.8 Hz), 3.11 (dd, 1H, *J* = 14.6, 3.6 Hz), 4.05 (dd, 1H, *J* = 16.7, 7.2 Hz), 4.15 (d, 1H, *J* = 15.6 Hz), 4.90 (d, 1H, *J* = 10.2 Hz), 5.00 (d, 1H, *J* = 17.2 Hz), 5.20 (d, 1H, *J* = 6.4 Hz), 6.76 (d, 2H, *J* = 7.6 Hz), 6.85 (d, 2H, *J* = 8.0 Hz), 7.15-7.43 (m, 11H), 7.59-7.69 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.0, 21.4, 22.4, 24.5, 31.3, 34.9, 46.9, 68.5, 82.2, 86.5, 90.8, 116.4, 122.3, 126.5, 126.6, 127.9, 128.3, 128.4, 128.6, 128.9, 129.0, 129.6, 132.1, 136.0, 137.4, 138.7, 139.3, 142.4; IR (NaCl, neat) *v*: 3019, 2231, 1751, 1215, 1155 cm^{-1}; HRMS (ESI) calcd. for $C_{39}H_{41}NO_4SNa$ (M^++Na): 642.2654, found: 642.2647.

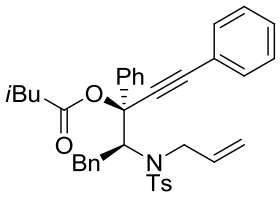
(3*S*,4*S*)-4-(*N*-Allyl-4-methylphenylsulfonamido)-1,3,5-triphenylpent-1-yn-3-yl 3-Phenylpropanoate (153j)



Yield 58%; 0.379 g; colourless solid, m.p. = 66-67 °C; $[\alpha]_D^{23}$ −15.5 (*c* 0.6, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.27 (s, 3H), 2.60-2.64 (m, 2H), 2.92 (t, 2H, *J* = 7.5 Hz),

3.02 (dd, 1H, *J* = 14.2, 9.7 Hz), 3.29 (dd, 1H, *J* = 14.7, 3.8 Hz), 3.99 (dd, 1H, *J* = 16.8, 7.2 Hz), 4.10 (d, 1H, *J* = 16.0 Hz), 4.89 (d, 1H, *J* = 10.2 Hz), 4.99 (d, 1H, *J* = 17.2 Hz), 5.13-5.15 (m, 1H), 5.57-5.59 (m, 1H), 6.77 (d, 2H, *J* = 7.7 Hz), 6.84 (d, 2H, *J* = 8.0 Hz), 7.08-7.35 (m, 16H), 7.53-7.61 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.4, 30.7, 34.7, 36.4, 46.9, 68.6, 82.6, 86.4, 90.8, 116.3, 122.2, 126.3, 126.5, 126.5, 127.9, 128.3, 128.3, 128.4, 128.4, 128.4, 128.6, 128.6, 129.0, 129.5, 132.2, 136.1, 137.3, 138.7, 139.1, 140.3, 142.4, 169.4; IR (NaCl, neat) *v*: 3026, 2234, 1753, 1155 cm^{-1}; HRMS (ESI) calcd. for $C_{42}H_{39}NO_4SNa$ (M^++Na): 676.2498, found: 676.2491.

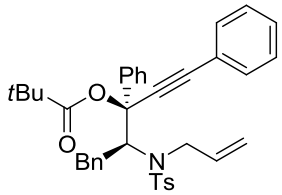
(3*S*,4*S*)-4-(*N*-Allyl-4-methylphenylsulfonamido)-1,3,5-triphenylpent-1-yn-3-yl 3-Methylbutanoate (153k)



Yield 72%; 0.436 g; colourless solid, m.p. = 102-104 °C; $[\alpha]_D^{23}$ −24.8 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.94-0.96 (m, 6H), 2.04-2.21 (m, 3H), 2.27 (s, 3H), 3.12 (dd, 1H, *J* = 14.2, 9.9 Hz), 3.44 (dd, 1H, *J* = 14.6, 3.6 Hz), 4.05 (dd, 1H, *J* = 16.7, 7.2 Hz), 4.14 (d, 1H, *J* = 14.4 Hz), 4.89 (d, 1H, *J* = 10.2 Hz), 4.99 (d, 1H, *J* = 17.2 Hz), 5.21-5.23 (m, 1H), 5.52-5.54 (m, 1H), 6.74 (d, 2H, *J* = 7.6 Hz), 6.85 (d, 2H, *J* = 8.0 Hz), 7.16-7.43 (m, 11H), 7.58-7.60 (m, 2H), 7.70 (d, 4H, *J* = 7.3 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.4, 22.4, 25.7, 35.0, 43.9, 46.9, 68.3, 82.2, 86.4, 90.8, 116.4, 122.2, 126.5, 126.7, 127.9, 128.4, 128.6, 128.9, 129.6, 132.0, 135.9, 137.4, 138.7, 139.3, 142.4, 169.6; IR (NaCl, neat) *v*: 3020, 1749, 1215, 1157 cm^{-1}; HRMS (ESI) calcd. for $C_{38}H_{39}NO_4SNa$ (M^++Na):

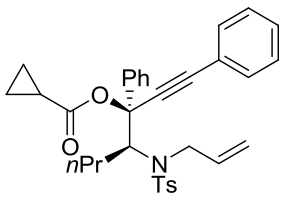
628.2498, found: 628.2496.

(3*S*,4*S*)-4-(*N*-Allyl-4-methylphenylsulfonamido)-1,3,5-triphenylpent-1-yn-3-yl Pivalate (153l)



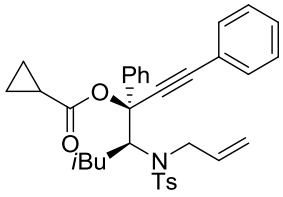
Yield 62%; 0.376 g; colourless solid, m.p. = 172-173 °C; $[\alpha]_D^{23}$ −45.2 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz): δ 1.31 (s, 9H), 2.28 (s, 3H), 3.20 (dd, 1H, *J* = 12.6, 10.7 Hz), 3.52 (d, 1H, *J* = 13.1 Hz), 4.09-4.24 (m, 2H), 4.91 (d, 1H, *J* = 10.1 Hz), 5.02 (d, 1H, *J* = 17.2 Hz), 5.33 (d, 1H, *J* = 8.7 Hz), 5.50-5.47(m, 1H), 6.69 (d, 2H, *J* = 7.9 Hz), 6.85 (d, 2H, *J* = 7.9 Hz), 7.23-7.50 (m, 11H), 7.63 (d, 2H, *J* = 3.5 Hz), 7.77 (d, 2H, *J* = 7.1 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 21.4, 27.1, 34.9, 39.3, 46.8, 68.7, 81.9, 86.3, 90.6, 116.6, 122.3, 126.6, 127.9, 128.4, 128.8, 128.9, 129.0, 129.7, 132.1, 135.7, 137.6, 138.5, 139.3, 142.4, 174.5; IR (NaCl, neat) *v*: 3019, 2234, 1746, 1630, 1215 cm^{-1}; HRMS (ESI) calcd. for $C_{38}H_{39}NO_4SNa$ (M^++Na): 628.2498, found: 628.2493.

(3*S*,4*S*)-4-(*N*-Allyl-4-methylphenylsulfonamido)-1,3-diphenylhept-1-yn-3-yl Cyclopropanecarboxylate (153m)



Yield 71%; 0.385 g; colourless solid, m.p. = 158-160 °C; $[\alpha]_D^{23}$ −35.4 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): δ 0.88-0.96 (m, 6H), 1.03-1.07 (m, 1H), 1.22-1.43 (m, 2H), 1.68-1.74 (m, 1H), 1.92-1.97 (m, 2H), 2.32 (s, 3H), 4.00-4.10 (m, 2H), 4.76 (t, 1H, *J* = 6.3 Hz), 4.90 (d, 1H, *J* = 10.2 Hz), 5.02 (d, 1H, *J* = 17.2 Hz), 5.69-5.77 (m, 1H), 7.04 (d, 2H, *J* = 8.1 Hz), 7.19 (d, 2H, *J* = 7.9 Hz), 7.29-7.42 (m, 6H), 7.51-7.53 (m, 2H), 7.63 (d, 2H, *J* = 6.9 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 8.3, 8.5, 13.7, 14.0, 20.0, 21.5, 30.0, 46.9, 66.2, 81.9, 86.8, 90.1, 116.4, 122.3, 126.5, 128.1, 128.2, 128.3, 128.4, 128.8, 129.0, 132.0, 135.9, 137.4, 139.9, 142.9, 171.2; IR (NaCl, neat) *v*: 2961, 2232, 1742, 1217 cm^{-1}; HRMS (ESI) calcd. for $C_{33}H_{35}NO_4SNa$ (M^++Na): 564.2185, found: 564.2188.

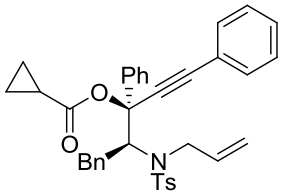
(3*S*,4*S*)-4-(*N*-Allyl-4-methylphenylsulfonamido)-6-methyl-1,3-diphenylhept-1-yn-3-yl Cyclopropanecarboxylate (153n)



Yield 78%; 0.434 g; colourless solid, m.p. = 167-168 °C; $[\alpha]_D^{23}$ −35.5 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): δ 0.89-1.08 (m, 10H), 1.68-1.76 (m, 3H), 2.04 (t, 1H, *J* = 11.4 Hz), 2.33 (s, 3H), 4.01 (dd, 1H *J* = 12.7, 4.1 Hz), 4.11 (dd, 1H, *J* = 16.9, 7.5 Hz), 4.89 (d, 2H, *J* = 10.5 Hz), 4.99 (d, 1H, *J* = 17.2 Hz), 5.62-5.72 (m, 1H), 7.05 (d, 2H, *J* = 8.0 Hz), 7.17 (d, 2H, *J* = 8.0 Hz), 7.32-7.43 (m, 6H), 7.52-7.54 (m, 2H), 7.66 (d, 2H, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 8.3, 8.5, 13.7, 21.5, 21.5, 23.7, 24.1, 37.3, 46.9,

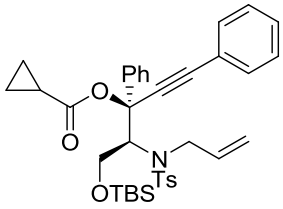
81.9, 86.8, 90.2, 116.3, 122.3, 126.5, 128.1, 128.3, 128.3, 128.4, 128.9, 129.1, 132.0, 135.9, 137.4, 139.9, 143.0, 171.2; IR (NaCl, neat) *v*: 3019, 2231, 1742, 1215 cm^{-1}; HRMS (ESI) calcd. for $C_{34}H_{37}NO_4SNa$ (M^++Na): 578.2341, found: 578.2350.

(3*S*,4*S*)-4-(*N*-Allyl-4-methylphenylsulfonamido)-1,3,5-triphenylpent-1-yn-3-yl Cyclopropanecarboxylate (153o)



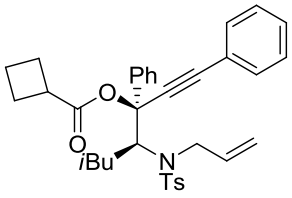
Yield 79%; 0.466 g; colourless solid, m.p. = 179-181 °C; $[\alpha]_D^{23}$ −1.5 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): δ 0.86-0.95 (m, 3H), 1.03-1.07 (m, 1H), 1.58-1.63 (m, 1H), 2.27 (s, 3H), 3.11 (dd, 1H, *J* = 14.2, 10.3 Hz), 3.41 (dd, 1H, *J* = 14.6, 3.0 Hz), 4.05 (dd, 1H, *J* = 16.7, 7.2 Hz), 4.16 (d, 1H, *J* = 13.8 Hz), 4.91 (d, 1H, *J* = 10.2 Hz), 5.01 (d, 1H, *J* = 17.2 Hz), 5.19 (d, 1H, *J* = 7.7 Hz), 5.58-5.60 (m, 1H), 6.76 (d, 2H, *J* = 7.6 Hz), 6.85 (d, 2H, *J* = 8.0 Hz), 7.12-7.43 (m, 11H), 7.60- 7.69 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 8.4, 8.6, 21.4, 34.6, 47.0, 68.9, 82.4, 86.6, 90.6, 116.4, 122.3, 126.5, 127.9, 128.3, 128.3, 128.4, 128.7, 128.9, 129.0, 129.6, 132.2, 136.1, 137.5, 138.7, 139.4, 142.4, 171.3; IR (NaCl, neat) *v*: 3019, 2234, 1742, 1215 cm^{-1}; HRMS (ESI) calcd. for $C_{37}H_{35}NO_4SNa$ (M^++Na): 612.2185, found: 612.2184.

(3*S*,4*S*)-4-(*N*-Allyl-4-methylphenylsulfonamido)-5-((*tert*-butyldimethylsilyl)oxy)-1,3-diphenylpent-1-yn-3-yl Cyclopropanecarboxylate (153p)



Yield 67%; 0.431 g; colourless solid, m.p. = 120-122 °C; $[\alpha]_D^{23}$ +3.7 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): δ 0.02 (s, 3H), 0.09 (s, 3H), 0.86-1.08 (m, 13H), 1.66-1.70 (m, 1H), 2.34 (s, 3H), 4.16-4.20 (m, 4H), 4.82 (d, 1H, *J* = 10.3 Hz), 4.92-4.97 (m, 2H), 5.65-5.75 (m, 1H), 7.07 (d, 2H, *J* = 8.0 Hz), 7.33-7.56 (m, 10H), 7.91 (d, 2H, *J* = 7.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ -5.8, -5.6, 8.4, 8.6, 13.6, 18.6, 21.5, 26.0, 47.0, 59.7, 67.9, 80.7, 86.1, 90.3, 115.7, 122.2, 126.3, 128.2, 128.3, 128.4, 128.5, 128.9, 128.9, 132.1, 136.0, 138.2, 139.2, 142.6, 171.1; IR (NaCl, neat) *v*: 2953, 2232, 1748, 1157 cm^{-1}; HRMS (ESI) calcd. for $C_{37}H_{45}NO_5SSiNa$ (M^++Na): 666.2685, found: 666.2688.

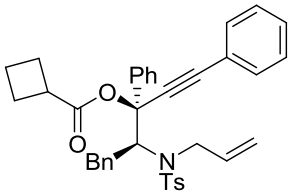
(3*S*,4*S*)-4-(*N*-Allyl-4-methylphenylsulfonamido)-6-methyl-1,3-diphenylhept-1-yn-3-yl Cyclobutanecarboxylate (153q)



Yield 52%; 0.296 g; colourless solid, m.p. = 143-144 °C; $[\alpha]_D^{23}$ −49.1 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): δ 0.95 (d, 3H, *J* = 5.8 Hz), 0.98 (d, 3H, *J* = 5.4 Hz), 1.67-1.76 (m, 2H), 1.87-2.06 (m, 3H), 2.18-2.39 (m, 7H), 3.19-3.27 (m, 1H), 3.99 (dd, 1H, *J* = 12.6, 4.2 Hz), 4.10 (dd, 1H, *J* = 16.9, 7.6 Hz), 4.85-4.98 (m, 3H), 5.58-5.67 (m, 1H), 7.03 (d,

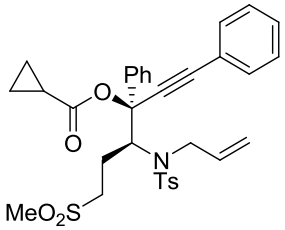
2H, *J* = 8.2 Hz), 7.11 (d, 2H, *J* = 8.2 Hz), 7.30-7.44 (m, 6H), 7.52-7.54 (m, 2H), 7.66 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 18.4, 21.5, 21.6, 23.7, 24.1, 24.9, 25.0, 37.5, 38.6, 46.9, 64.1, 81.6, 86.6, 90.3, 116.3, 122.2, 126.6, 128.1, 128.3, 128.3, 128.4, 128.9, 129.0, 132.0, 135.8, 137.3, 139.9, 143.0, 171.7; IR (NaCl, neat) *v*: 2955, 2232, 1749, 1155 cm^{-1}; HRMS (ESI) calcd. for $C_{35}H_{39}NO_4SNa$ (M^++Na): 592.2498, found: 592.2495.

(3*S*,4*S*)-4-(*N*-Allyl-4-methylphenylsulfonamido)-1,3,5-triphenylpent-1-yn-3-yl Cyclobutanecarboxylate (153r)



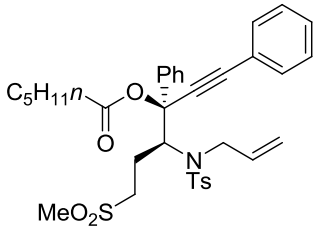
Yield 66%; 0.398 g; colourless solid, m.p. = 74-76 °C; $[\alpha]_D^{23}$ −16.2 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.87-2.04 (m, 2H), 2.14-2.34 (m, 7H), 3.06-3.18 (m, 2H), 3.40 (dd, 1H, *J* = 14.7, 3.4 Hz), 4.05 (dd, 1H, *J* = 16.6, 7.4 Hz), 4.15 (d, 1H, *J* = 16.6 Hz), 4.89 (d, 1H, *J* = 10.2 Hz), 5.00 (d, 1H, *J* = 17.2 Hz), 5.20 (d, 1H, *J* = 7.2 Hz), 5.52-5.54 (m, 1H), 6.73 (d, 2H, *J* = 7.8 Hz), 6.84 (d, 2H, *J* = 8.1 Hz), 7.13-7.26 (m, 5H), 7.32-7.44 (m, 6H), 7.59-7.62 (m, 2H), 7.69 (d, 2H, *J* = 7.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 18.4, 21.4, 24.8, 25.1, 34.8, 38.5, 46.9, 68.6, 86.5, 90.6, 116.4, 122.3, 126.5, 126.5, 127.9, 128.3, 128.4, 128.6, 128.9, 129.6, 132.1, 135.9, 137.5, 138.6, 139.4, 142.4, 171.7; IR (NaCl, neat) *v*: 3020, 2236, 1746, 1638, 1215 cm^{-1}; HRMS (ESI) calcd. for $C_{38}H_{37}NO_4SNa$ (M^++Na): 626.2341, found: 626.2335.

(3*S*,4*S*)-4-(*N*-Allyl-4-methylphenylsulfonamido)-6-(methylsulfonyl)-1,3-diphenylhex-1-yn-3-yl Cyclopropanecarboxylate (153s)



Yield 52%; 0.315 g; colourless solid, m.p. = 71-73 °C; $[\alpha]_D^{23}$ −51.7 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): δ 0.87-1.01 (m, 4H), 1.66-1.71 (m, 1H), 2.27 (s, 3H), 2.63-2.72 (m, 2H), 2.90 (s, 3H), 3.06-3.13 (m, 1H), 3.19-3.27 (m, 1H), 4.00 (d, 1H, *J* = 15.6 Hz), 4.19 (dd, 1H, *J* = 16.5, 8.0 Hz), 4.80 (s, 1H), 4.98 (d, 1H, *J* = 10.1 Hz), 5.08 (d, 1H, *J* = 17.2 Hz), 5.73-5.83 (m, 1H), 6.96-7.02 (m, 4H), 7.27-7.43 (m, 8H), 7.58 (d, 2H, *J* = 5.3 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 8.6, 8.8, 13.5, 20.6, 21.5, 41.3, 47.0, 52.1, 64.8, 81.2, 85.5, 91.1, 118.0, 121.6, 126.2, 128.1, 128.3, 128.4, 128.7, 129.1, 129.3, 131.9, 134.8, 136.3, 139.3, 143.5, 171.0; IR (NaCl, neat) *v*: 3022, 2232, 1746, 1152 cm^{-1}; HRMS (ESI) calcd. for $C_{33}H_{35}NO_6S_2Na$ (M^++Na): 628.1804, found: 628.1815.

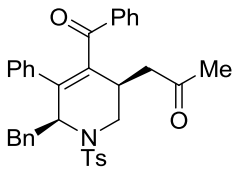
(3*S*,4*S*)-4-(*N*-Allyl-4-methylphenylsulfonamido)-6-(methylsulfonyl)-1,3-diphenylhex-1-yn-3-yl Hexanoate (153t):



Yield 55%; 0.350 g; yellow oil; $[\alpha]_D^{23}$ −74.0 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): δ 0.87 (t, 3H, *J* = 6.8 Hz), 1.28-1.33 (m, 4H), 1.58-1.65 (m, 2H), 2.28 (s, 3H), 2.37 (td,

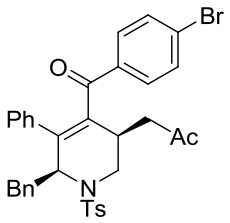
2H, *J* = 7.5, 2.3 Hz), 2.61-2.67 (m, 2H), 2.91 (s, 3H), 3.07-3.15 (m, 1H), 3.21-3.29 (m, 1H), 3.98 (d, 1H, *J* = 15.6 Hz), 4.17 (d, 1H, *J* = 16.6, 8.2 Hz), 4.80 (s, 1H), 4.96 (d, 1H, *J* = 10.2 Hz), 5.06 (d, 1H, *J* = 17.2 Hz), 5.70-5.76 (m, 1H), 6.98 (s, 4H), 7.28-7.44 (m, 8H), 7.59-7.60 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 13.9, 20.6, 21.5, 22.3, 24.4, 31.2, 34.8, 41.3, 47.0, 52.1, 64.5, 81.1, 85.3, 91.3, 118.1, 121.6, 126.4, 128.1, 128.4, 128.5, 128.7, 129.2, 129.3, 131.9, 134.7, 136.2, 139.3, 143.6, 170.0; IR (NaCl, neat) *v*: 3024, 2229, 1755, 1317, 1217, 1153 cm−1; HRMS (ESI) calcd. for $C_{35}H_{41}NO_6S_2Na$ (M^++Na): 658.2273, found: 658.2266.

1-((3*R*,6*S*)-4-Benzoyl-6-benzyl-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-3 yl)propan-2-one (156a)



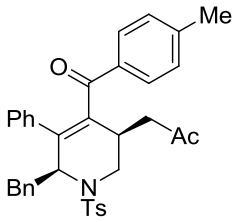
Yield 75%; 0.085 g; colourless solid, m.p. = 143-145 °C; $[\alpha]_D^{23}$ +103.4 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.13 (s, 3H), 2.41 (s, 3H), 2.48 (dd, 1H, *J* = 18.2, 7.1 Hz), 2.74 (dd, 1H, *J* = 18.2, 4.6 Hz), 2.85-2.87 (m, 2H), 3.08 (dd, 1H, *J* = 14.4, 11.0 Hz), 3.19-3.26 (m, 1H), 3.92 (dd, 1H, *J* = 14.4, 6.2 Hz), 4.99 (t, 1H, *J* = 6.5 Hz), 6.98-7.01 (m, 2H), 7.07-7.20 (m, 12H), 7.33-7.48 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.6, 30.4, 30.8, 38.1, 42.5, 44.0, 58.1, 126.4, 127.6, 128.0, 128.2, 128.3, 129.0, 129.2, 129.4, 129.6, 133.1, 136.1, 136.4, 136.9, 137.6, 137.7, 139.6, 143.2, 198.3, 206.0; IR (NaCl, neat) *v*: 3021, 1717, 1659, 1597, 1215 cm^{-1}; HRMS (ESI) calcd. for $C_{35}H_{34}NO_4S$ (M^++H): 564.2209, found: 564.2218.

1-((3*R*,6*S*)-6-Benzyl-4-(4-bromobenzoyl)-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-3-yl)propan-2-one (156b)



Yield 66%; 0.085 g; yellow solid, m.p. = 74-76 °C; $[\alpha]_D^{23}$ +62.7 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.13 (s, 3H), 2.41 (s, 3H), 2.48 (dd, 1H, *J* = 18.2, 6.4 Hz), 2.72-2.89 (m, 3H), 3.10 (dd, 1H, *J* = 14.2, 11.0 Hz), 3.20-3.26 (m, 1H), 3.91 (dd, 1H, *J* = 14.4, 6.2 Hz), 4.93-4.96 (m, 1H), 6.95-6.97 (m, 2H), 7.09-7.17 (m, 10H), 7.31-7.37 (m, 4H), 7.43 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.6, 30.4, 30.7, 38.0, 42.5, 43.9, 58.1, 126.4, 127.6, 128.3, 128.3, 128.5, 128.9, 129.3, 129.6, 130.6, 131.6, 134.9, 136.0, 136.6, 137.5, 137.5, 139.9, 143.3, 197.4, 206.0; IR (NaCl, neat) *v*: 1717, 1663 cm^{-1}; HRMS (ESI) calcd. for $C_{35}H_{33}NO_4S^{79}Br$ (M^++H): 642.1314, found: 642.1323.

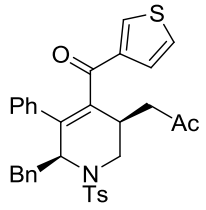
1-((3*R*,6*S*)-6-Benzyl-4-(4-methylbenzoyl)-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-3-yl)propan-2-one (156c)



Yield 74%; 0.086 g; pale yellow solid, m.p. = 80-82 °C; $[\alpha]_D^{23}$ +91.5 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.10 (s, 3H), 2.27 (s, 3H), 2.40-2.46 (m, 4H), 2.72 (dd, 1H, *J* = 18.2, 4.6 Hz), 2.82-2.90 (m, 2H), 3.04 (dd, 1H, *J* = 14.4, 11.0 Hz), 3.16-3.23 (m, 2H), 3.93 (dd, 1H, *J* = 14.4, 6.3 Hz), 4.99 (t, 1H, *J* = 6.6 Hz), 6.98-7.01 (m, 4H), 7.08-7.21 (m,

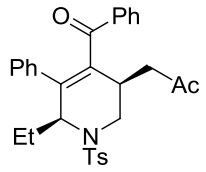
10H), 7.40 (d, 2H, *J* = 8.0 Hz), 7.47 (d, 2H, *J* = 8.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.6, 21.7, 30.4, 30.8, 38.1, 42.5, 44.1, 58.0, 126.4, 127.6, 128.0, 128.3, 129.0, 129.1, 129.4, 129.5, 129.6, 133.5, 136.6, 136.9, 137.6, 137.8, 138.9, 143.2, 144.1, 197.8, 206.0; IR (NaCl, neat) *v*: 1717, 1603 cm^{-1}; HRMS (ESI) calcd. for $C_{36}H_{36}NO_4S$ (M^++H): 578.2365, found: 578.2375.

1-((3*R*,6*S*)-6-Benzyl-5-phenyl-4-(thiophene-3-carbonyl)-1-tosyl-1,2,3,6-tetrahydropyridin-3-yl)propan-2-one (156d)



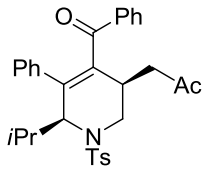
Yield 53%; 0.061 g; yellow oil; $[\alpha]_D^{23}$ +71.4 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.15 (s, 3H), 2.40 (s, 3H), 2.51 (dd, 1H, *J* = 18.2, 7.2 Hz), 2.73-2.90 (m, 3H), 3.12 (dd, 1H, *J* = 14.0, 11.4 Hz), 3.26-3.27 (m, 1H), 3.97 (dd, 1H, *J* = 14.5, 6.4 Hz), 4.93 (t, 1H, *J* = 5.3 Hz), 6.95-7.03 (m, 3H), 7.14-7.21 (m, 11H), 7.44 (d, 2H, *J* = 7.8 Hz), 7.59 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.6, 30.4, 30.8, 37.9, 42.4, 44.1, 58.1, 126.1, 126.3, 126.7, 127.6, 128.1, 128.3, 128.4, 128.9, 129.3, 129.7, 135.9, 136.7, 137.2, 137.6, 137.8, 139.2, 141.4, 143.4, 191.8, 206.1; IR (NaCl, neat) *v*: 1717, 1651 cm^{-1}; HRMS (ESI) calcd. for $C_{33}H_{32}NO_4S_2$ (M^++H): 570.1773, found: 570.1774.

1-((3*R*,6*S*)-4-Benzoyl-6-ethyl-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-3-yl)propan-2-one (156e)



Yield 61%; 0.061 g; colourlesss oil; $[\alpha]_D^{23}$ +198.9 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.86 (t, 3H, *J* = 7.3 Hz), 1.48-1.62 (m, 1H), 2.10 (s, 3H), 2.42-2.49 (m, 4H), 2.75 (dd, 1H, *J* = 18.2, 4.8 Hz), 3.01-3.17 (m, 2H), 4.20 (dd, 1H, *J* = 14.0, 5.6 Hz), 4.50 (d, 1H, *J* = 7.0 Hz), 6.97-7.15 (m, 9H), 7.30 (t, 1H, *J* = 7.2 Hz), 7.44 (m, 2H, *J* = 8.0 Hz), 7.99 (d, 2H, *J* = 8.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 11.0, 21.7, 25.3, 30.3, 30.3, 42.7, 44.1, 58.3, 127.5, 127.8, 128.0, 128.1, 128.8, 128.9, 130.0, 133.0, 135.4, 136.2, 137.8, 138.3, 140.3, 143.5, 198.2, 205.9; IR (NaCl, neat) *v*: 1717, 1657 cm^{-1}; HRMS (ESI) calcd. for $C_{30}H_{32}NO_4S$ (M^++H): 502.2052, found: 502.2047.

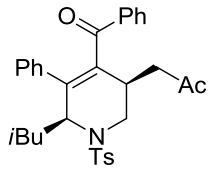
1-((3*R*,6*S*)-4-Benzoyl-6-isopropyl-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-3-yl)propan-2-one (156f)



Yield 73%; 0.075 g; colourless solid, m.p. = 101-102 °C; $[\alpha]_D^{23}$ +187.5 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.88 (d, 3H, *J* = 6.7 Hz), 0.92 (d, 3H, *J* = 7.0 Hz), 1.80-1.88 (m, 1H), 2.09 (s, 3H), 2.42 (dd, 1H, *J* = 18.3, 7.4 Hz), 2.49 (s, 3H), 2.81 (dd, 1H, *J* = 18.3, 4.8 Hz), 2.99 (m, 1H), 3.15 (dd, 1H, *J* = 14.8, 11.0 Hz), 4.26 (dd, 1H, *J* = 14.7, 6.4 Hz), 4.59 (d, 1H, *J* = 4.6 Hz), 7.00-7.16 (m, 9H), 7.30 (t, 1H, *J* = 7.2 Hz), 7.44 (m, 2H, *J*

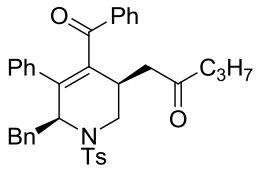
= 8.0 Hz), 8.00 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 19.3, 20.6, 21.7, 29.8, 30.3, 31.9, 44.7, 44.9, 61.0, 127.7, 127.7, 128.0, 128.1, 128.8, 128.9, 130.0, 132.9, 136.0, 137.0, 138.1, 138.6, 139.0, 143.5, 198.4, 205.8; IR (NaCl, neat) *v*: 1719, 1655 cm^{-1}; HRMS (ESI) calcd. for $C_{31}H_{34}NO_4S$ (M^++H): 516.2209, found: 516.2200.

1-((3*R*,6*S*)-4-Benzoyl-6-isobutyl-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-3-yl)propan-2-one (156g)



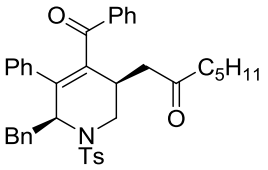
Yield 60%; 0.064 g; Colourless solid, m.p. = 137-138 °C; $[\alpha]_D^{23}$ +174.4 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.70 (d, 3H, *J* = 6.4 Hz), 0.81 (d, 3H, *J* = 6.6 Hz), 1.05-1.12 (m, 1H), 1.61-1.75 (m, 2H), 2.10 (s, 3H), 2.43-2.48 (m, 4H), 2.77 (dd, 1H, *J* = 18.2, 4.6 Hz), 3.07-3.20 (m, 2H), 4.11-4.17 (m, 1H), 4.67 (d, 1H, *J* = 10.3 Hz), 6.98-7.10 (m, 7H), 7.17 (d, 2H, *J* = 7.4 Hz), 7.29 (t, 1H, *J* = 7.3 Hz), 7.44 (m, 2H, *J* = 8.1 Hz), 7.99 (d, 2H, *J* = 8.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 20.9, 21.7, 23.6, 24.4, 30.1, 30.3, 41.3, 42.5, 44.2, 127.7, 127.8, 128.0, 128.1, 128.8, 129.0, 130.0, 132.9, 135.2, 136.2, 137.8, 138.0, 140.6, 143.6, 198.3, 205.9; IR (NaCl, neat) *v*: 1717, 1657 cm^{-1}; HRMS (ESI) calcd. for $C_{32}H_{36}NO_4S$ (M^++H): 530.2365, found: 530.2358.

1-((3*R*,6*S*)-4-Benzoyl-6-benzyl-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-3-yl)pentan-2-one (156h)



Yield 67%; 0.079 g; colourless solid, m.p. = 147-148 °C; $[\alpha]_D^{23}$ +112.4 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, MHz): δ 0.88 (t, 3H, *J* = 7.4 Hz), 1.50-1.59 (m, 2H), 2.31-2.43 (m, 6H), 2.70 (dd, 1H, *J* = 18.0, 4.7 Hz), 2.83-2.90 (m, 2H), 3.04 (dd, 1H, *J* = 14.4, 11.0 Hz), 3.19-3.25 (m, 1H), 3.93 (dd, 1H, *J* = 14.5, 6.2 Hz), 4.98 (t, 1H, *J* = 6.5 Hz), 7.00-7.19 (m, 13H), 7.25-7.35 (m, 2H), 7.43-7.49 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 13.7, 17.1, 21.6, 30.8, 38.2, 42.7, 43.3, 45.0, 58.1, 126.4, 127.6, 128.0, 128.2, 128.3, 129.1, 129.2, 129.5, 129.6, 133.1, 136.1, 136.6, 137.0, 137.6, 137.7, 139.4, 143.2, 198.2, 208.3; IR (NaCl, neat) *v*: 3022, 1713, 1661, 1217 cm^{-1}; HRMS (ESI) calcd. for $C_{37}H_{38}NO_4S$ (M^++H): 592.2522, found: 592.2528.

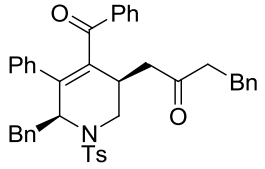
1-((3*R*,6*S*)-4-Benzoyl-6-benzyl-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-3-yl)heptan-2-one (156i)



Yield 77%; 0.096 g; yellow oil; $[\alpha]_D^{23}$ +89.5 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.88 (t, 3H, *J* = 7.2 Hz), 1.19-1.32 (m, 4H), 1.48-1.55 (m, 2H), 2.34-2.43 (m, 6H), 2.70 (dd, 1H, *J* = 18.0, 4.6 Hz), 2.85-2.90 (m, 2H), 3.03 (dd, 1H, *J* = 14.3, 11.0 Hz), 3.21-3.23 (m, 1H), 3.93 (dd, 1H, *J* = 14.6, 6.2 Hz), 4.98 (d, 1H, *J* = 6.4 Hz), 7.00-7.19 (m, 14H),

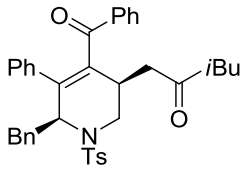
7.32-7.35 (m, 1H), 7.43-7.49 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 13.9, 21.6, 22.4, 23.3, 30.8, 31.3, 38.2, 42.7, 43.1, 43.3, 58.1, 126.4, 127.6, 128.0, 128.2, 128.3, 129.1, 129.2, 129.5, 129.6, 129.6, 133.1, 136.1, 136.6, 137.0, 137.6, 137.7, 139.4, 143.2, 198.2, 208.4; IR (NaCl, neat) *v*: 1713, 1661 cm^{-1}; HRMS (ESI) calcd. for $C_{39}H_{42}NO_4S$ (M^++H): 620.2835, found: 620.2825.

1-((3*R*,6*S*)-4-Benzoyl-6-benzyl-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-3-yl)-4-phenylbutan-2-one (156j)



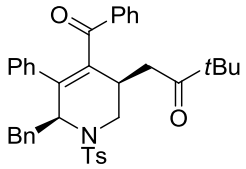
Yield 69%; 0.090 g; colourlesss oil; $[\alpha]_D^{23}$ +93.5 (*c* 0.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.36-2.42 (m, 4H), 2.65-2.73 (m, 3H), 2.79-2.88 (m, 4H), 3.02 (dd, 1H, *J* = 14.5, 11.0 Hz), 3.20-3.25 (m, 1H), 3.89 (dd, 1H, *J* = 14.5, 6.3 Hz), 4.97 (t, 1H, *J* = 6.6 Hz), 6.97-7.29 (m, 19H), 7.32-7.35 (m, 1H), 7.44-7.47 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.6, 29.7, 30.8, 38.1, 42.6, 43.5, 44.6, 58.1, 126.1, 126.4, 127.6, 128.1, 128.2, 128.3, 128.5, 129.0, 129.2, 129.5, 129.6, 133.2, 136.1, 136.4, 136.9, 137.6, 137.7, 139.6, 140.9, 143.2, 198.2, 207.3; IR (NaCl, neat) *v*: 1717, 1653 cm^{-1}; HRMS (ESI) calcd. for $C_{42}H_{40}NO_4S$ (M^++H): 654.2678, found: 654.2680.

1-((3*R*,6*S*)-4-Benzoyl-6-benzyl-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-3-yl)-4-methylpentan-2-one (156k)



Yield 64%; 0.078 g; Colourless solid, m.p. = 161-162 °C; $[\alpha]_D^{23}$ +110.8 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.86-0.90 (m, 6H), 2.02-2.12 (m, 1H), 2.24-2.26 (m, 2H), 2.34-2.41 (m, 4H), 2.69 (dd, 1H, *J* = 18.1, 4.7 Hz), 2.85 (d, 2H, *J* = 6.6 Hz), 3.01 (dd, 1H, *J* = 14.5, 11.0 Hz), 3.19- 3.25 (m, 1H), 3.94 (dd, 1H, *J* = 14.5, 6.3 Hz), 4.98 (t, 1H, *J* = 6.6 Hz), 7.01-7.20 (m, 14H), 7.34 (t, 1H, *J* = 7.3 Hz), 7.44 (d, 2H, *J* = 7.6 Hz), 7.49 (d, 2H, *J* = 8.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.6, 22.5, 22.6, 24.4, 30.7, 38.2, 42.7, 43.9, 52.1, 58.0, 126.4, 127.6, 128.0, 128.2, 128.3, 129.1, 129.2, 129.5, 129.6, 133.1, 136.1, 136.7, 137.0, 137.6, 137.7, 139.4, 143.2, 198.2, 207.9; IR (NaCl, neat) *v*: 2957, 1713, 1661, 1155 cm^{-1}; HRMS (ESI) calcd. for $C_{38}H_{40}NO_4S$ (M^++H): 606.2678, found: 606.2678.

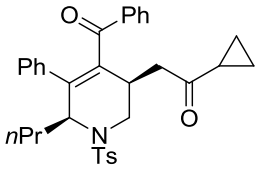
1-((3*R*,6*S*)-4-Benzoyl-6-benzyl-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-3-yl)-3,3-dimethylbutan-2-one (156l)



Yield 22%; 0.027 g; colourless solid, m.p. = 187-188 °C; $[\alpha]_D^{23}$ +110.7 (*c* 0.75, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.08 (s, 9H), 2.43-2.50 (m, 4H), 2.71-2.91 (m, 4H), 3.17-

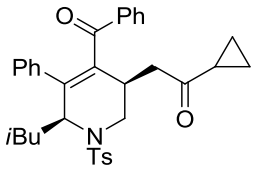
3.19 (m, 1H), 3.96 (dd, 1H, *J* = 14.6, 6.3 Hz), 4.98 (t, 1H, *J* = 6.0 Hz), 7.02-7.26 (m, 14H), 7.32-7.38 (m, 3H), 7.57 (d, 2H, *J* = 8.2 Hz); 13C NMR (CDCl3, 100 MHz): δ 21.3, 26.5, 30.4, 38.1, 38.4, 42.8, 44.1, 58.0, 126.5, 127.5, 128.0, 128.2, 128.3, 129.1, 129.6, 129.7, 133.1, 136.0, 137.2, 137.3, 137.5, 137.7, 139.0, 143.2, 197.9, 213.2; IR (NaCl, neat) *v*: 3021, 1703, 1661, 1157 cm^{-1}; HRMS (ESI) calcd. for $C_{38}H_{40}NO_4S$ (M^++H): 606.2678, found: 606.2668.

2-((3*R*,6*S*)-4-Benzoyl-5-phenyl-6-propyl-1-tosyl-1,2,3,6-tetrahydropyridin-3-yl)-1-cyclopropylethanone (156m)



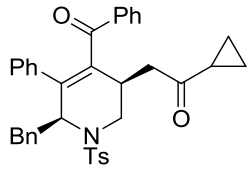
Yield 72%; 0.078 g; yellow oil; $[\alpha]_D^{23}$ +162.3 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.77-1.02 (m, 7H), 1.21-1.60 (m, 4H), 1.83-1.89 (m, 1H), 2.48 (s, 3H), 2.60 (dd, 1H, *J* = 18.1, 6.9 Hz), 2.88 (dd, 1H, *J* = 18.1, 4.0 Hz), 3.10 (dd, 2H, *J* = 19.3, 10.6 Hz), 4.23 (dd, 1H, *J* = 19.8, 11.4 Hz), 4.59 (d, 2H, *J* = 9.2 Hz), 6.98-7.14 (m, 9H), 7.30 (t, 1H, *J* = 7.2 Hz), 7.43 (d, 2H, *J* = 8.1 Hz), 7.99 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 10.8, 11.0, 13.6, 19.6, 20.8, 21.7, 30.0, 34.4, 42.8, 44.5, 56.8, 127.5, 127.8, 128.0, 128.1, 128.9, 128.9, 130.0, 133.0, 135.6, 136.1, 137.8, 138.3, 140.1, 143.4, 197.8, 207.9; IR (NaCl, neat) *v*: 1697, 1661 cm^{-1}; HRMS (ESI) calcd. for $C_{33}H_{36}NO_4S$ (M^++H): 542.2365, found: 542.2366.

2-((3*R*,6*S*)-4-Benzoyl-6-isobutyl-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-3-yl)-1-cyclopropylethanone (156n)



Yield 70%; 0.078 g; colourless solid, m.p. = 173-174 °C; $[\alpha]_D^{23}$ +163.6 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.71 (d, 3H, *J* = 6.4 Hz), 0.81-0.94 (m, 6H), 0.98-1.01 (m, 1H), 1.07-1.14 (m, 1H), 1.58-1.65 (m, 1H), 1.71-1.77 (m, 1H), 1.84-1.90 (m, 1H), 2.48 (s, 3H), 2.59 (dd, 1H *J* = 17.9, 7.6 Hz), 2.91 (dd, 1H *J* = 17.9, 4.3 Hz), 3.05-3.11 (m, 2H), 4.19 (d, 1H, *J* = 8.8 Hz), 4.68 (d, 1H, *J* = 10.4 Hz), 6.99-7.10 (m, 7H), 7.17 (d, 2H, *J* = 7.2 Hz), 7.30 (t, 2H, *J* = 7.3 Hz), 7.42 (m, 2H, *J* = 8.1 Hz), 7.99 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 10.8, 11.0, 20.8, 20.9, 21.7, 23.7, 24.4, 30.0, 41.4, 42.6, 44.6, 55.1, 127.6, 127.8, 128.0, 128.1, 128.8, 129.0, 130.0, 132.9, 135.5, 136.1, 137.8, 138.1, 140.4, 143.5, 197.9, 208.0; IR (NaCl, neat) *v*: 1697, 1659 cm^{-1}; HRMS (ESI) calcd. for $C_{34}H_{38}NO_4S$ (M^++H): 556.2522, found: 556.2522.

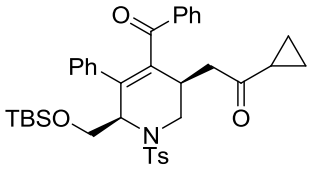
2-((3*R*,6*S*)-4-Benzoyl-6-benzyl-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-3-yl)-1-cyclopropylethanone (156o)



Yield 72%; 0.085 g; colourless solid, m.p. = 177-178 °C; $[\alpha]_D^{23}$ +111.0 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.85-0.95 (m, 3H), 1.00-1.03 (m, 1H), 1.85-1.91 (m, 1H),

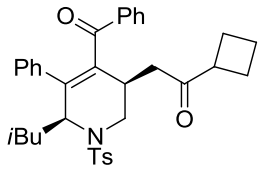
2.40 (s, 3H), 2.58 (dd, 1H, *J* = 17.8, 8.0 Hz), 2.80-3.01 (m, 4H), 3.24-3.28 (m, 1H), 3.98 (dd, 1H, *J* = 14.7, 6.3 Hz), 4.99 (t, 1H, *J* = 7.2 Hz), 7.00-7.20 (m, 14H), 7.35 (t, 1H, *J* = 7.2 Hz), 7.48 (d, 4H, *J* = 8.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 10.8, 11.1, 20.8, 21.6, 30.7, 38.2, 42.7, 44.4, 126.4, 127.6, 128.0, 128.2, 128.3, 129.1, 129.2, 129.5, 129.6, 133.2, 136.0, 136.8, 137.0, 137.6, 137.7, 139.4, 143.2, 197.9, 208.0; IR (NaCl, neat) *v*: 1697, 1663 cm^{-1}; HRMS (ESI) calcd. for $C_{37}H_{36}NO_4S$ (M^++H): 590.2365, found: 590.2359.

2-((3*R*,6*R*)-4-Benzoyl-6-(((*tert*-butyldimethylsilyl)oxy)methyl)-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-3-yl)-1-cyclopropylethanone (156p)



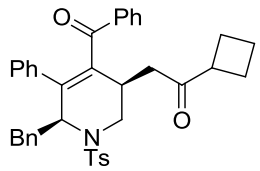
Yield 66%; 0.085 g; colourless solid, m.p. = 125-126 °C; $[\alpha]_D^{23}$ +121.0 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ -0.07 (s, 3H), -0.02 (s, 3H), 0.81-0.90 (m, 12H), 0.95-0.90 (m, 1H), 1.80-1.87 (m, 1H), 2.48-2.56 (m, 4H), 2.87 (dd, 1H, *J* = 17.8, 5.2 Hz), 3.06-3.10 (m, 1H), 3.46 (dd, 1H, *J* = 14.1, 10.9 Hz), 3.58 (dd, 1H, *J* = 10.5, 3.8 Hz), 3.79 (dd, 1H, *J* = 10.6, 2.4 Hz), 4.20 (dd, 1H, *J* = 14.1, 6.0 Hz), 4.65 (s, 1H), 6.98-7.34 (m, 10H), 7.42 (d, 2H, *J* = 8.1 Hz), 7.96 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ -5.7, -5.6, 18.2, 20.8, 21.7, 25.9, 30.3, 44.3, 45.1, 58.1, 64.9, 127.3, 127.9, 128.0, 128.9, 129.1, 130.0, 133.0, 136.1, 136.3, 137.2, 138.3, 138.6, 143.4, 197.8, 207.9; IR (NaCl, neat) *v*: 1697, 1661 cm^{-1}; HRMS (ESI) calcd. for $C_{37}H_{46}NO_5SSi$ (M^++H): 644.2866, found: 644.2861.

2-((3*R*,6*S*)-4-Benzoyl-6-isobutyl-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-3-yl)-1-cyclobutylethanone (156q)



Yield 64%; 0.073 g; colourless solid, m.p. = 189-191°C ; $[\alpha]_D^{23}$ +172.0 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.71 (d, 3H, *J* = 6.4 Hz), 0.82 (d, 3H, *J* = 6.7 Hz), 1.07-1.13 (m, 1H), 1.63-1.66 (m, 1H), 1.73-1.78 (m, 2H), 1.82-1.99 (m, 1H), 2.04-2.21 (m, 4H), 2.38 (dd, 1H *J* = 18.2, 6.6 Hz), 2.49 (s, 3H), 2.66 (dd, 1H *J* = 18.3, 3.7 Hz), 3.06-3.23 (m, 3H), 3.05-3.11 (m, 2H), 4.18 (dd, 1H, *J* = 19.8, 11.6 Hz), 4.68 (d, 1H, *J* = 10.1 Hz), 6.98-7.15 (m, 9H), 7.30 (t, 1H, *J* = 7.2 Hz), 7.44 (m, 2H, *J* = 8.0 Hz), 8.02 (d, 2H, *J* = 8.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 17.7, 20.9, 21.8, 23.7, 24.1, 24.4, 24.7, 29.7, 40.9, 41.4, 42.7, 45.5, 55.2, 127.6, 127.8, 128.0, 128.1, 128.8, 129.0, 130.0, 132.9, 135.5, 136.1, 137.8, 138.2, 140.4, 143.5, 198.0, 209.1; IR (NaCl, neat) *v*: 1707, 1659 cm^{-1}; HRMS (ESI) calcd. for $C_{35}H_{40}NO_4S$ (M^++H): 570.2678, found: 570.2677.

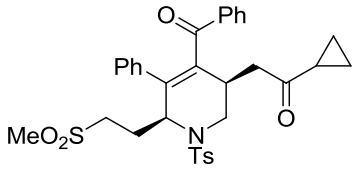
2-((3*R*,6*S*)-4-Benzoyl-6-benzyl-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-3-yl)-1-cyclobutylethanone (156r)



Yield 65%; 0.079 g; colourless solid, m.p. = 173-175 °C; $[\alpha]_D^{23}$ +117.1 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.74-1.83 (m, 1H), 1.88-2.00 (m, 1H), 2.07-2.25 (m, 4H), 2.31-2.41 (m, 4H), 2.62 (dd, 1H, *J* = 18.2, 4.4 Hz), 2.86 (d, 2H, *J* = 6.6 Hz), 3.00 (dd, 1H,

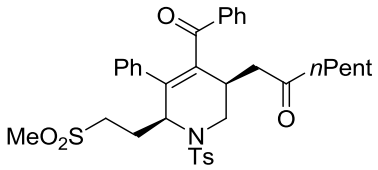
J = 14.4, 11.0 Hz), 3.15-3.24 (m, 2H), 3.95 (dd, 1H, *J* = 14.5, 6.3 Hz), 4.99 (t, 1H, *J* = 6.5 Hz), 7.01-7.21 (m, 14H), 7.34 (t, 1H, *J* = 7.3 Hz), 7.44 (d, 2H, *J* = 7.6 Hz), 7.50 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 17.7, 21.6, 24.2, 24.6, 30.5, 38.2, 40.7, 42.7, 45.5, 58.1, 126.4, 127.6, 128.0, 128.2, 128.3, 129.1, 129.1, 129.5, 129.7, 133.1, 136.1, 136.8, 137.0, 137.6, 137.7, 139.4, 143.2, 198.0, 209.2; IR (NaCl, neat) *v*: 1705, 1659 cm^{-1}; HRMS (ESI) calcd. for $C_{38}H_{38}NO_4S$ (M^++H): 604.2522, found: 604.2526.

2-((3*R*,6*S*)-4-Benzoyl-6-(2-(methylsulfonyl)ethyl)-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-3-yl)-1-cyclopropylethanone (156s)



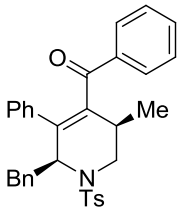
Yield 67%; 0.081 g; colourless solid, m.p. = 195-197 °C; $[\alpha]_D^{23}$ +183.2 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.84-1.01 (m, 4H), 1.83-1.89 (m, 1H), 1.99-2.04 (m, 1H), 2.11-2.17 (m, 1H), 2.52 (s, 3H), 2.61 (dd, 1H, *J* = 18.1, 7.5 Hz), 2.80-2.87 (m, 4H), 3.01-3.17 (m, 3H), 3.23-3.31(m, 3H), 4.32 (dd, 1H, *J* = 17.8, 4.8 Hz), 4.66 (dd, 1H, *J* = 10.5 Hz), 6.91-6.95 (m, 4H), 7.01-7.10 (m, 5H), 7.29 (t, 1H, *J* = 7.3 Hz), 7.49 (d, 2H, *J* = 8.0 Hz), 8.01 (d, 2H, *J* = 8.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 11.0, 11.1, 20.9, 21.8, 23.7, 29.7, 41.4, 42.8, 43.9, 51.7, 55.6, 127.4, 128.0, 128.3, 128.4, 128.7, 128.8, 130.3, 133.1, 135.8, 136.6, 137.1, 137.8, 137.9, 144.0, 197.0, 207.7; IR (NaCl, neat) *v*: 1697, 1661 cm^{-1}; HRMS (ESI) calcd. for $C_{33}H_{36}NO_6S_2$ (M^++H): 606.1984, found: 606.1980.

1-((3*R*,6*S*)-4-Benzoyl-6-(2-(methylsulfonyl)ethyl)-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-3-yl)heptan-2-one (156t)



Yield 62%; 0.079 g; colourless solid, m.p. = 105-107 °C; $[\alpha]_D^{23}$ +179.7 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.87 (t, 3H, *J* = 7.2 Hz), 1.19-1.31 (m, 5H), 1.46-1.53 (m, 2H), 1.96-2.02 (m, 1H), 2.11-2.20 (m, 1H), 2.32-2.44 (m, 3H), 2.53 (s, 3H), 2.69 (dd, 1H, *J* = 18.2, 4.8 Hz), 2.87 (s, 3H), 3.01-3.17 (m, 3H), 3.27 (td, 1H, *J* = 10.7, 4.2 Hz), 4.29 (dd, 1H, *J* = 14.3, 5.4 Hz), 4.68 (d, 1H, *J* = 10.2 Hz), 6.90-6.93 (m, 4H), 7.00-7.09 (m, 5H), 7.29 (t, 1H, *J* = 7.4 Hz), 7.50 (d, 2H, *J* = 8.2 Hz), 8.02 (d, 2H, *J* = 8.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 13.9, 21.8, 22.4, 23.3, 23.7, 29.7, 31.3, 41.4, 42.8, 43.0, 43.1, 51.7, 55.6, 127.5, 128.0, 128.4, 128.5, 128.7, 130.3, 133.1, 135.8, 136.6, 137.0, 137.8, 137.9, 144.1, 197.3, 208.1; IR (NaCl, neat) *v*: 2930, 1711, 1659, 1313, 1161 cm^{-1}; HRMS (ESI) calcd. for $C_{35}H_{42}NO_6S_2$ (M^++H): 636.2454, found: 636.2457.

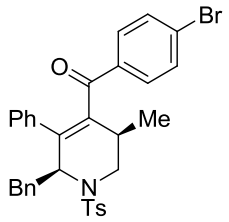
((3*R*,6*S*)-6-Benzyl-3-methyl-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-4-yl)(phenyl)methanone (157a)



Yield 96%; 0.100 g; Colourless solid, m.p. = 146-148 °C; $[\alpha]_D^{23}$ +47.7 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.96 (d, 3H, *J* = 6.5 Hz), 2.40 (s, 3H), 2.75 (dd, 1H, *J* = 14.2,

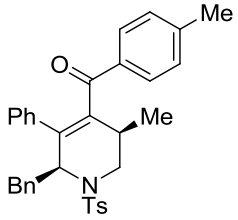
9.5 Hz), 2.82-2.93(m, 3H), 3.80-3.89 (m, 1H), 4.91 (dd, 1H, *J* = 9.4, 3.8 Hz), 6.93-6.95 (m, 2H), 7.12-7.28 (m, 12H), 7.38-7.42 (m, 3H), 7.63 (d, 1H, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 16.5, 21.6, 30.1, 38.3, 44.8, 58.4, 126.3, 127.5, 127.8, 128.2, 128.3, 128.4, 129.2, 129.3, 129.3, 129.6, 133.2, 135.9, 136.9, 137.5, 137.8, 138.1, 139.4, 143.1, 197.3; IR (NaCl, neat) *v*: 3019, 1665, 1215 cm^{-1}; HRMS (ESI) calcd. for $C_{33}H_{32}NO_3S$ (M^++H): 522.2103, found: 522.2095.

((3*R*,6*S*)-6-Benzyl-3-methyl-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-4-yl)(4-bromophenyl)methanone (157b):



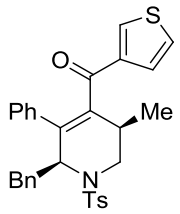
Yield 88%; 0.106 g; pale yellow solid, mp = 146-148 °C; $[\alpha]_D^{23}$ +5.9 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.98 (d, 3H, *J* = 6.6 Hz), 2.40 (s, 3H), 2.71-2.95 (m, 4H), 3.86 (dd, 1H, *J* = 14.0, 5.3 Hz), 4.87 (dd, 1H, *J* = 9.5, 3.8 Hz), 6.92 (d, 2H, *J* = 7.8 Hz), 7.10-7.28 (m, 10H), 7.37 (d, 2H, *J* = 8.2 Hz), 7.41 (d, 2H, *J* = 8.6 Hz), 7.52 (d, 2H, *J* = 8.6 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 16.5, 21.6, 30.1, 38.2, 44.7, 58.4, 126.4, 127.6, 128.1, 128.3, 128.4, 128.6, 129.1, 129.3, 129.6, 130.8, 131.8, 134.6, 136.6, 137.4, 137.6, 138.6, 138.9, 143.2, 196.3; IR (NaCl, neat) *v*: 3021, 1667, 1215, 1153 cm^{-1}; HRMS (ESI) calcd. for $C_{33}H_{31}NO_3S^{79}Br$ (M^++H): 600.1208, found: 600.1208.

((3*R*,6*S*)-6-Benzyl-3-methyl-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-4-yl)(*p*-tolyl)methanone (157c)



Yield 93%; 0.1 g; yellow oil; $[\alpha]_D^{23}$ +28.3 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): δ 0.96 (d, 3H, *J* = 6.3 Hz), 2.31 (s, 3H), 2.41 (s, 3H), 2.73-2.93 (m, 4H), 3.86 (dd, 1H, *J* = 13.6, 4.9 Hz), 4.93 (dd, 1H, *J* = 8.9, 3.1 Hz), 6.96 (d, 2H, *J* = 5.9 Hz), 7.06-7.31 (m, 12H), 7.41 (d, 2H, *J* = 8.0 Hz), 7.54 (d, 2H, *J* = 7.9 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 16.5, 21.6, 21.7, 30.2, 38.3, 44.8, 58.4, 126.3, 127.5, 127.8, 128.2, 128.3, 129.2, 129.4, 129.5, 129.6, 133.4, 137.0, 137.6, 137.6, 137.9, 139.5, 143.1, 144.1, 196.9; IR (NaCl, neat) *v*: 3026, 1663, 1217 cm^{-1}; HRMS (ESI) calcd. for $C_{34}H_{34}NO_3S$ (M^++H): 536.2259, found: 536.2261.

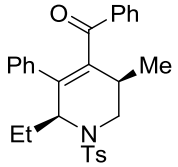
((3*R*,6*S*)-6-Benzyl-3-methyl-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-4-yl)(thiophen-3-yl)methanone (157d)



Yield 91%; 0.096 g; colourless solid, mp = 155-157 °C; $[\alpha]_D^{23}$ +16.0 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): δ 1.02 (d, 3H, *J* = 6.2 Hz), 2.40 (s, 3H), 2.73 (dd, 1H, *J* = 14.2, 9.6 Hz), 2.83 (dd, 1H, *J* = 14.2, 3.9 Hz), 2.89-2.97 (m, 2H), 3.91 (dd, 1H, *J* = 20.2, 11.5 Hz), 4.83 (dd, 1H, *J* = 9.5, 3.8 Hz), 6.91 (d, 2H, *J* = 6.4 Hz), 7.06-7.29 (m, 12H), 7.40 (d,

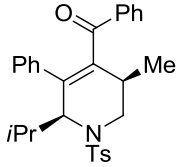
2H, *J* = 8.2 Hz), 7.70 (d, 1H, *J* = 2.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 16.6, 21.6, 30.2, 38.2, 44.7, 58.5, 126.2, 126.3, 126.8, 127.6, 127.9, 128.3, 128.3, 129.1, 129.2, 129.6, 135.6, 136.7, 137.5, 137.6, 137.8, 140.1, 141.3, 143.3, 191.0; IR (NaCl, neat) *v*: 3025, 1655, 1153 cm^{-1}; HRMS (ESI) calcd. for $C_{31}H_{30}NO_3S_2$ (M^++H): 528.1667, found: 528.1667.

((3*R*,6*S*)-6-Ethyl-3-methyl-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-4-yl)(phenyl)methanone (157e)



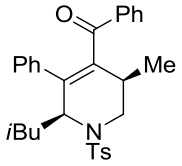
Yield 97%; 0.089 g; yellow oil; $[\alpha]_D^{23}$ +105.8 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.82 (t, 3H, *J* = 7.3 Hz), 0.92 (d, 3H, *J* = 6.9 Hz), 1.54-1.59 (m, 2H), 2.43 (s, 3H), 2.50-2.66 (m, 1H), 3.02 (dd, 1H, *J* = 14.7, 11.3 Hz), 4.10 (dd, 1H, *J* = 14.8, 6.1 Hz), 4.42-4.45 (m, 1H), 7.07-7.42 (m, 12H), 7.93 (d, 2H, *J* = 8.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 11.1, 16.4, 21.7, 25.4, 29.7, 44.9, 58.6, 127.5, 127.6, 128.0, 128.2, 129.0, 129.0, 129.9, 133.0, 136.0, 137.9, 138.3, 138.3, 138.8, 143.4, 197.3; IR (NaCl, neat) *v*: 3019, 1663, 1157 cm^{-1}; HRMS (ESI) calcd. for $C_{28}H_{30}NO_3S$ (M^++H): 460.1946, found: 460.1942.

((3*R*,6*S*)-6-Isopropyl-3-methyl-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-4-yl)(phenyl)methanone (157f)



Yield 87%; 0.082 g; yellow oil; $[\alpha]_D^{23}$ +172.0 (*c* 1.0, CHCl3); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.87-0.95 (m,9H), 1.81-1.87 (m, 1H), 2.50 (s, 3H), 3.10 (dd, 1H, *J* = 15.0, 11.2 Hz), 4.11 (dd, 1H, *J* = 15.0, 6.5 Hz), 4.56 (d, 1H, *J* = 4.3 Hz), 7.03-7.17 (m, 7H), 7.29-7.37 (m, 3H), 7.42 (d, 2H, *J* = 8.1 Hz), 7.93 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 16.7, 19.2, 20.6, 21.7, 29.1, 31.8, 47.1, 61.3, 127.6, 128.0, 128.2, 128.9, 129.0, 130.0, 133.0, 135.8, 137.4, 138.3, 138.5, 139.7, 143.4, 197.4; IR (NaCl, neat) *v*: 3021, 1665, 1161 cm^{-1}; HRMS (ESI) calcd. for $C_{29}H_{32}NO_3S$ (M^++H): 474.2103, found: 474.2116.

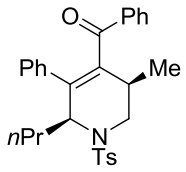
((3*R*,6*S*)-6-Isobutyl-3-methyl-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-4-yl)(phenyl)methanone (157g)



Yield 97%; 0.095 g; colourlesss oil; $[\alpha]_D^{23}$ +100.4 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.64 (d, 3H, *J* = 6.4 Hz), 0.81 (d, 3H, *J* = 6.7 Hz), 0.94 (d, 3H, *J* = 6.9 Hz), 1.14-1.27 (m, 1H), 1.57-1.72 (m, 2H), 2.50 (s, 3H), 2.62-2.68 (m, 1H). 3.02-3.08 (m,1H), 4.04 (dd, 1H, *J* = 14.9, 6.1 Hz), 4.95 (d, 1H, *J* = 10.5 Hz), 7.06-7.18 (m, 7H), 7.33-7.42 (m, 5H), 7.93 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 16.5, 20.8, 21.7, 23.7, 24.4,

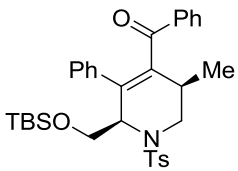
29.5, 41.6, 44.7, 55.4, 127.6, 128.0, 128.2, 129.0, 129.1, 129.9, 133.0, 136.0, 137.9, 138.1, 139.1, 143.5, 197.3; IR (NaCl, neat) *v*: 3019, 1663, 1217 cm^{-1}; HRMS (ESI) calcd. for $C_{30}H_{34}NO_3S$ (M^++H): 488.2259, found: 488.2267.

((3*R*,6*S*)-3-Methyl-5-phenyl-6-propyl-1-tosyl-1,2,3,6-tetrahydropyridin-4-yl)(phenyl)methanone (157m)



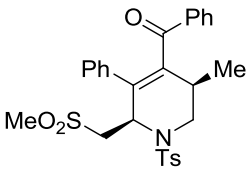
Yield 97%; 0.092 g; colourless solid, mp = 143-144 °C; $[\alpha]_D^{23}$ +128.4 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.75 (t, 3H, *J* = 7.2 Hz), 0.92 (d, 3H, *J* = 6.9 Hz), 1.11-1.21 (m, 1H), 1.38-1.61 (m, 3H), 2.50 (s, 3H), 2.57-2.66 (m, 1H), 3.04 (dd, 1H, *J* = 14.8, 11.3 Hz), 4.09 (dd, 1H, *J* = 14.8, 6.2 Hz), 4.52 (d, 1H, *J* = 9.6 Hz), 7.07-7.18 (m, 7H), 7.31-7.42 (m, 5H), 7.92 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 13.6, 16.4, 19.6, 21.7, 29.6, 34.5, 44.9, 57.1, 127.5, 127.6, 129.0, 128.2, 129.0, 129.0, 129.9, 133.0, 136.0, 137.9, 138.2, 138.3, 138.9, 143.4, 197.3; IR (NaCl, neat) *v*: 3019, 2399, 1663, 1159 cm^{-1}; HRMS (ESI) calcd. for $C_{29}H_{32}NO_3S$ (M^++H): 474.2103, found: 474.2105.

((3*R*,6*R*)-6-(((tert-Butyldimethylsilyl)oxy)methyl)-3-methyl-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-4-yl)(phenyl)methanone (157p)



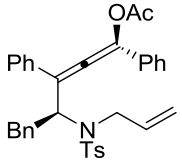
Yield 52%; 0.06 g; yellow solid, mp = 96-98 °C; $[\alpha]_D^{23}$ +91.1 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): δ -0.04 (s, 3H), -0.03 (s, 3H), 0.90 (s, 12H), 2.50 (s, 3H), 2.61-2.62 (m, 1H), 3.46 (dd, 1H, *J* = 14.0, 11.2 Hz), 3.64 (dd, 1H, *J* = 10.6, 3.6 Hz), 3.76 (d, 1H, *J* = 10.6 Hz), 4.07 (dd, 1H, *J* = 14.2, 6.0 Hz), 4.60 (s, 1H), 7.05-7.10 (m, 5H), 7.19 (t, 2H, *J* = 7.6 Hz), 7.36-7.43 (m, 5H), 7.88 (t, 2H, *J* = 8.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ -5.7, -5.6, 16.1, 18.2, 21.7, 25.9, 30.1, 47.1, 58.4, 64.6, 127.2, 127.7, 127.9, 128.2, 129.0, 129.2, 129.9, 133.0, 134.9, 136.4, 137.3, 138.4, 140.9, 143.3, 197.3; IR (NaCl, neat) *v*: 1665 cm^{-1}; HRMS (ESI) calcd. for $C_{33}H_{42}NO_4SSi$ (M^++H): 576.2604, found: 576.2593.

((3*R*,6*S*)-3-Methyl-6-(2-(methylsulfonyl)ethyl)-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-4-yl)(phenyl)methanone (157s)



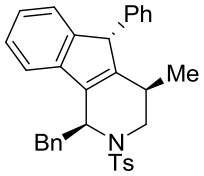
Yield 87%; 0.094 g; colourless solid, mp = 93-95 °C; $[\alpha]_D^{23}$ +159.1 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): δ 0.92 (d, 3H, *J* = 6.9 Hz), 2.04-2.17 (m, 2H), 2.48-2.55 (m, 4H), 1.96-2.02 (m, 1H), 2.11-2.20 (m, 1H), 2.32-2.44 (m, 3H), 2.99 (s, 3H), 3.02-3.12 (m, 2H), 3.21-3.27 (m, 1H), 4.18 (dd, 1H, *J* = 15.1, 6.0 Hz), 4.62 (d, 1H, *J* = 7.2 Hz), 6.98-7.00 (m, 2H), 7.09-7.15 (m, 7H), 7.34-7.38 (m, 1H), 7.48 (d, 2H, *J* = 8.2 Hz), 7.93 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 16.2, 21.8, 23.8, 29.3, 41.3, 44.8, 51.7, 55.9, 127.3, 128.2, 128.4, 128.8, 128.9, 130.3, 133.2, 135.7, 136.6, 136.8, 137.8, 139.6, 144.1, 196.4; IR (NaCl, neat) *v*: 3019, 1661 cm^{-1}; HRMS (ESI) calcd. for $C_{29}H_{32}NO_5S_2$ (M^++H): 538.1722, found: 538.1721.

(2*R*,4*S*)-4-(*N*-Allyl-4-methylphenylsulfonamido)-1,3,5-triphenylpenta-1,2-dienyl Acetate (154a)



Yield 87%; 0.094 g; colourlesss oil; $[\alpha]_D^{23}$ −18.0 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.14 (s, 3H), 2.36 (s, 3H), 3.04 (dd, 1H, *J* = 14.0, 4.7 Hz), 3.19 (dd, 1H, *J* = 14.0, 9.8 Hz), 3.82-3.95 (m, 2H), 4.89-4.93 (m, 2H), 5.56-5.66 (m, 1H), 5.73 (dd, 1H, *J* = 9.8, 4.7 Hz), 7.09-7.38 (m, 15H), 7.46-7.52 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 20.7, 21.5, 39.6, 46.5, 59.5, 116.8, 118.9, 124.8, 126.4, 127.3, 127.5, 127.8, 128.4, 128.5, 128.6, 128.7, 128.8, 129.3, 129.4, 132.1, 134.4, 135.6, 137.4, 137.8, 143.2, 167.9, 200.4; IR (NaCl, neat) *v*: 3019, 2399, 1755, 1215, 1157 cm^{-1}; HRMS (ESI) calcd. For $C_{35}H_{34}NO_4S$ (M^++H): 564.2209, found: 564.2196.

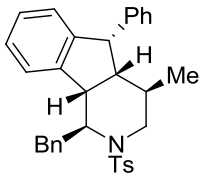
(1*S*,4*R*,5*S*)-1-Benzyl-4-methyl-5-phenyl-2-tosyl-2,3,4,5-tetrahydro-1*H*-indeno[1,2-c]pyridine (166)



Yield 94%; 0.143 g; colourless solid, mp = 85-87 °C; $[\alpha]_D^{23}$ +107.4 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.74 (d, 3H, *J* = 6.8 Hz), 2.13-2.22 (m, 1H), 2.37 (s, 3H), 2.49 (dd, 1H, *J* = 14.6, 11.0 Hz), 3.19 (dd, 1H, *J* = 14.0, 7.0 Hz), 3.35 (dd, 1H, *J* = 13.9, 4.5 Hz), 3.82 (dd, 1H, *J* = 14.7, 6.2 Hz), 4.42 (s, 1H), 5.30 (s, 1H), 6.62 (d, 2H, *J* = 6.3 Hz), 7.10-7.17 (m, 2H), 7.24-7.31 (m, 5H), 7.51 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$,

100 MHz): δ 17.0, 21.6, 27.0, 40.2, 46.1, 54.2, 55.4, 118.8, 123.9, 125.3, 126.7, 126.8, 126.9, 127.9, 128.3, 128.7, 129.7, 130.0, 136.1, 137.5, 138.3, 138.5, 141.6, 142.7, 148.2, 148.2; IR (NaCl, neat) *v*: 3019, 1599, 1337, 1215, 1159 cm^{-1}; HRMS (ESI) calcd. for $C_{33}H_{32}NO_2S$ (M^++H): 506.2154, found: 506.2159.

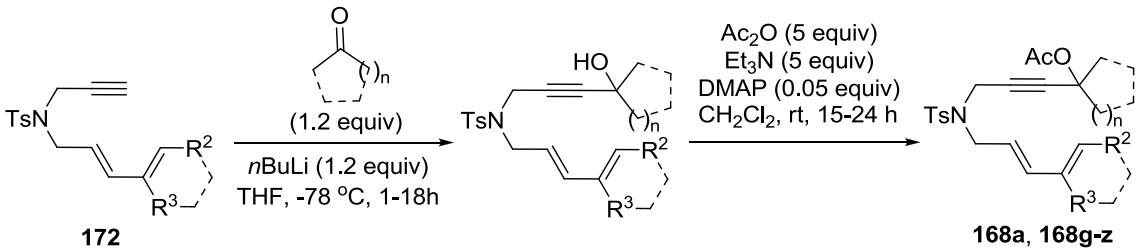
(1*S*,4*R*,4a*R*,5*S*,9b*S*)-1-Benzyl-4-methyl-5-phenyl-2-tosyl-2,3,4,4a,5,9b-hexahydro-1*H*-indeno[1,2-c]pyridine (167)



Yield 91%; 0.092 g; Colourlesss oil; $[\alpha]_D^{23}$ −127.3 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.12 (d, 3H, *J* = 6.2 Hz), 1.62-1.69 (m, 1H), 2.52 (s, 3H), 2.68-2.75 (m, 2H), 2.93 (dd, 1H, *J* = 13.2, 3.9 Hz), 3.08 (t, 1H, *J* = 12.1 Hz), 3.27 (d, 1H, *J* = 5.8 Hz), 3.46 (dd, 1H, *J* = 13.2, 5.6 Hz), 4.56 (d, 1H, *J* = 5.8 Hz), 5.09 (dd, 1H, *J* = 10.8, 3.6 Hz), 7.23-7.48 (m, 16H), 7.72 (d, 2H, *J* = 8.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 18.2, 21.5, 26.7, 36.7, 45.4, 45.7, 50.2, 53.5, 54.7, 123.0, 125.1, 126.6, 126.7, 127.1, 127.3, 128.5, 128.8, 129.2, 129.6, 129.9, 137.8, 138.4, 139.6, 143.0, 143.6, 144.0; IR (NaCl, neat) *v*: 3019, 2399, 1601, 1497, 1341, 1215, 1157 cm^{-1}. HRMS (ESI) calcd. for $C_{33}H_{34}NO_2S$ (M^++H): 508.2310, found: 508.2313.

7.3 Gold Catalyzed Cycloisomerization of 1,6,8-Dienyne Carbonates and Esters to *cis*-Cyclohepta-4,8-diene-fused Pyrrolidines

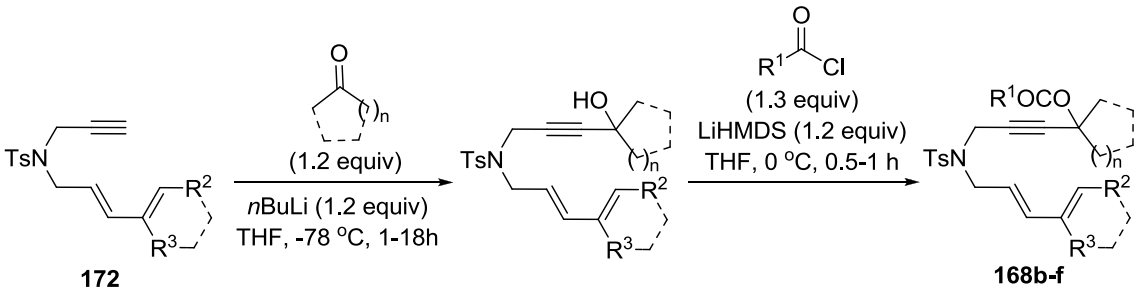
General Experimental Procedure for the Preparation of 168a, 168g-z



To a stirred solution of the appropriate (E)-4-methyl-N-(penta-2,4-dienyl)-N-(prop-2-ynyl)benzenesulfonamide **172** (5.0 mmol) in THF (20 mL) was added *n*butyllithium (2.4 mL, 6.0 mmol, 2.5 M in cyclohexane) at −78 °C. The resulting solution was stirred at −78 °C for 1 hour. A solution of respective ketone (6.0 mmol) in THF (10 mL) was subsequently slowly added to the resulting solution at −78 °C and the reaction mixture was stirred overnight. The reaction mixture was then quenched with saturated NH_4Cl (15 mL) and extracted with EtOAc (3 x 15 mL). The combined organic layers were washed with brine (15 mL), dried over $MgSO_4$, concentrated under reduced pressure and purified by flash column chromatography on silica gel with *n*Hex:EtOAc = 5:1 as eluent to furnish 1,6,8-dienyne alcohols which, without characterisation, were directly employed in the next reaction. The resulting alcohol was dissolved in 15 mL of CH_2Cl_2, triethylamine (5 equiv), DMAP (0.05 equiv) and acetic anhydride (5 equiv) were then added and the resulting solution was stirred at room temperature for 15-24 hours. Upon completion indicated by TLC analysis, the reaction mixture was quenched by addition of 1N NaOH (10 mL) and extracted with CH_2Cl_2 (2x 15 mL). The combined organic layers were washed with brine (15 mL), dried over $MgSO_4$, concentrated under reduced pressure and

purified by flash column chromatography on silica gel with *n*Hex:EtOAc: = 9:1 as eluent to yield the desired product **168a, 168g-z** in 36-81% yield over 2 steps.

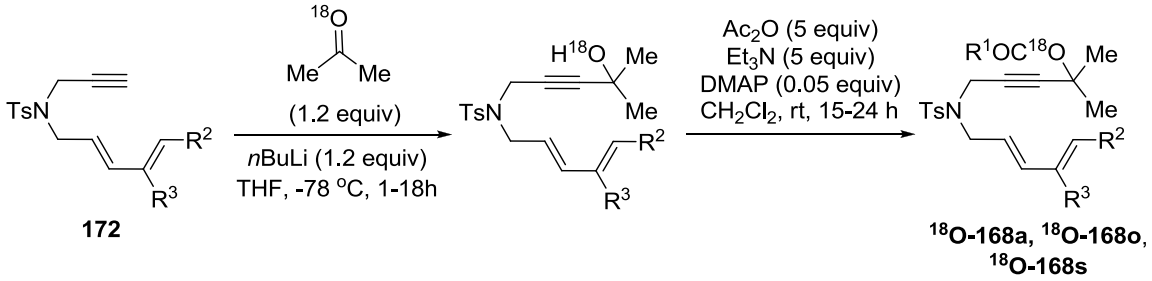
General Experimental Procedure for the Preparation of 168b-f



To a stirred solution of the appropriate (E)-4-methyl-N-(penta-2,4-dienyl)-N-(prop-2-ynyl)benzenesulfonamide **172** (5.0 mmol) in THF (20 mL) was added *n*butyllithium (2.4 mL, 6.0 mmol, 2.5 M in cyclohexane) at −78 °C. The resulting solution was stirred at −78 °C for 1 hour. A solution of respective ketone (6.0 mmol) in THF (10 mL) was subsequently slowly added to the resulting solution at −78 °C and the reaction mixture was stirred overnight. The reaction mixture was then quenched with saturated NH_4Cl (15 mL) and extracted with EtOAc (3 x 15 mL). The combined organic layers were washed with brine (15 mL), dried over $MgSO_4$, concentrated under reduced pressure and purified by flash column chromatography on silica gel with *n*Hex:EtOAc = 5:1 as eluent to furnish 1,6,8-dienyne alcohols which, without characterisation, were directly employed in the next reaction. To a solution of the resulting alcohol (1 mmol) in anhydrous THF (8 mL), LiHMDS (1.2 mL, 1.2 mmol, 1.0 M in THF) was added under a nitrogen condition at room temperature. The reaction solution was stirred for a further 30 min at room temperature, then R^3COCl (1.3 mmol) was added and the reaction mixture was stirred at room temperature for 45 min. Upon completion as indicated by TLC analysis, the

reaction mixture was quenched with saturated NH_4Cl (10 mL) and extracted with EtOAc (2 x 15 mL). The combined organic layers were washed with brine (10 mL), dried over $MgSO_4$, concentrated under reduced pressure and purified by flash column chromatography on silica gel with *n*Hex:EtOAc = 9:1 as eluent to furnish 1,6,8-dienyne esters **168b-f** in 43-77% yield over 2 steps.

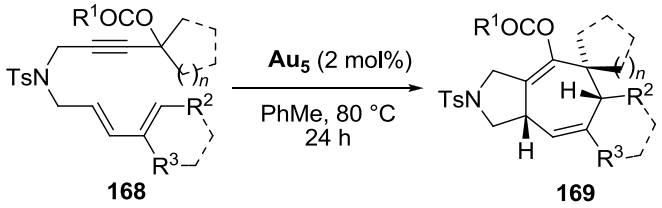
General Experimental Procedure for the Preparation of ^{18}O-168a, ^{18}O-168o and ^{18}O-168s from 172



To a stirred solution of the appropriate (E)-4-methyl-N-(penta-2,4-dienyl)-N-(prop-2-ynyl)benzenesulfonamide **172** (2.0 mmol) in THF (10 mL) was added *n*butyllithium (0.96 mL, 2.4 mmol, 2.5 M in cyclohexane) at −78 °C. The resulting solution was stirred at −78 °C for 1 hour. A solution of ^{18}O-acetone (90% ^{18}O content) (2.4 mmol) in THF (3 mL) was subsequently slowly added to the resulting solution at −78 °C and the reaction mixture was stirred overnight. The reaction mixture was then quenched with saturated NH_4Cl (10 mL) and extracted with EtOAc (3 x 10 mL). The combined organic layers were washed with brine (10 mL), dried over $MgSO_4$, concentrated under reduced pressure and purified by flash column chromatography on silica gel with *n*Hex:EtOAc = 5:1 as eluent to furnish 1,6,8-dienyne alcohols which, without characterisation, were directly employed in the next reaction. The resulting alcohol was dissolved in 10 mL of

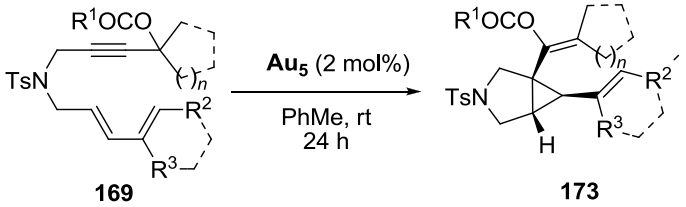
CH_2Cl_2, triethylamine (5 equiv), DMAP (0.05 equiv) and acetic anhydride (5 equiv) were then added and the resulting solution was stirred at room temperature for 15-24 hours. Upon completion (indicated by TLC analysis), the reaction mixture was quenched by addition of 1N NaOH (8 mL) and extracted with CH_2Cl_2 (2x 10 mL). The combined organic layers were washed with brine (10 mL), dried over $MgSO_4$, concentrated under reduced pressure and purified by flash column chromatography on silica gel with *n*Hex:EtOAc: = 9:1 as eluent to yield the desired product ^{18}O-**168a**, ^{18}O-**168o**, ^{18}O-**168s** in 55%, 57%, 66% yield over 2 steps, respectively.

General Experimental Procedure for Gold(I) Phosphine Complex Au_5-Catalyzed Cycloisomerization of 1,6,8-Dienyne Carbonates and Esters 168 to *cis*-Cyclohepta-4,8-diene-fused Pyrrolidine Derivatives 169



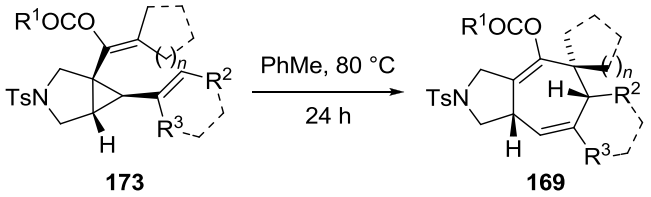
To a solution of 1,6,8-dienyne carbonate or ester **168** (0.2 mmol) in toluene (2 mL) was added gold(I) phosphine complex **Au_5** (4 μmol). The reaction mixture was stirred at 80 °C for 24 h. The reaction mixture was then cooled to room temperature, filtered through Celite, washed with CH_2Cl_2 (10 mL) and concentrated under reduced pressure. Purification by flash column chromatography on silica gel with *n*Hex/EtOAc = 9:1 as eluent gave the title compound.

General Experimental Procedure for Control Reactions with ^{18}O-168a, 168k and 168m



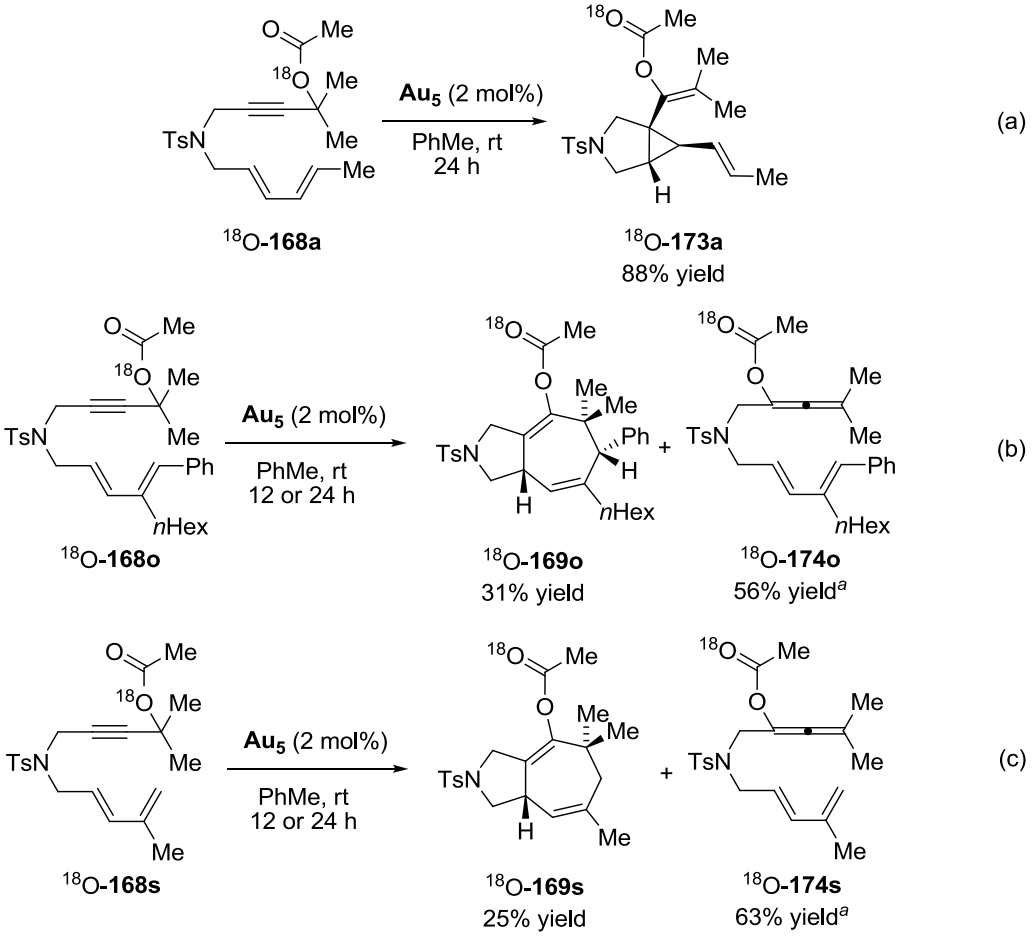
To a solution of 1,6,8-dienyne ester ^{18}O-**168a** or **168k** or **168m** (0.2 mmol) in toluene (2 mL) was added gold(I) complex **Au$_5$** (4 μmol). The reaction mixture was stirred at room temperature for 24 h (**Caution:** reaction temperature should be less than 25 °C). The reaction mixture was concentrated under reduced pressure. Purification by flash column chromatography on silica gel with *n*Hex/EtOAc = 9:1 as eluent gave ^{18}O-**173a** (88% yield), **169k** (21% yield) with **173k** (73% yield), or **173m** (88% yield), respectively.

General Experimental Procedure for Control Reactions with 173a, ^{18}O-173a, 173k and 173m



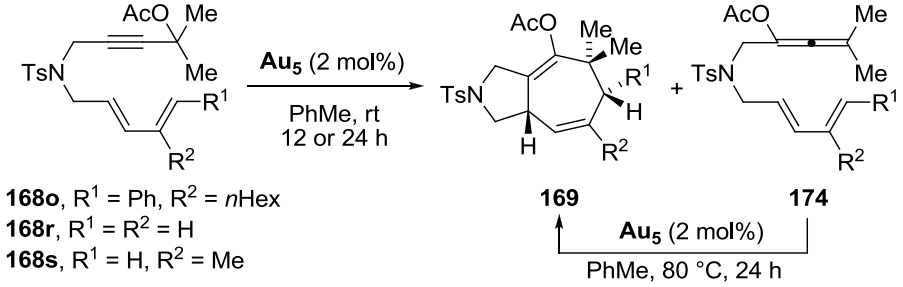
A solution of **173a** or ^{18}O-**173a** or **173k** or **173m** (0.1 mmol) in toluene (1 mL) was heated at 80 °C for 24 h. The reaction mixture was then cooled to room temperature and purified by flash column chromatography on silica gel with *n*Hex/EtOAc = 9:1 as eluent to give **169a** (90% yield), ^{18}O-**169a** (95% yield), **169k** (96% yield) and **169m** (92% yield), respectively.

General Experimental Procedure for Control Reactions with 168o, ^{18}O-168o, 168r, 168s and ^{18}O-168s



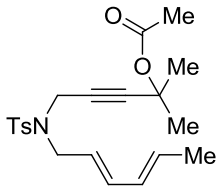
To a solution of 1,6,8-dienyne ester **168o** or ^{18}O-**168o** or **168r** or **168s** or ^{18}O-**168s** (0.2 mmol) and 4Å MS (100 mg) in toluene (2 mL) was added gold(I) complex **Au$_5$** (4 μmol). The reaction mixture was stirred at room temperature for 12 or 24 h. The reaction mixture was then filtered through Celite, washed with CH_2Cl_2 (10 mL) and concentrated under reduced pressure. Purification by flash column chromatography on silica gel with *n*Hex/EtOAc = 9:1 as eluent gave the product **169** and allene adduct **174** or the latter as an inseparable mixture with the substrate.

General Experimental Procedure for Control Reactions with 168o+174o, ^{18}O-168o+^{18}O-174o, 168r+174r, 168s+174s and ^{18}O-168s+^{18}O-174s



To a solution of **168o**+**174o** or ^{18}O-**168o**+^{18}O-**174o** or **168r**+**174r** or **168s**+**174s** or ^{18}O-**168s**+^{18}O-**174s** (0.1 mmol) and 4Å MS (100 mg) in toluene (1 mL) was added gold(I) complex **Au$_5$** (2 μmol). The reaction mixture was stirred at 80 °C for 24 h. The reaction mixture was then filtered through Celite, washed with CH_2Cl_2 (5 mL) and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (nhexane/EtOAc = 9:1 as eluent) gave **169o** (72% yield), ^{18}O-**169o** (72% yield), **169r** (71% yield), **169s** (79% yield) and ^{18}O-**169s** (81% yield), respectively.

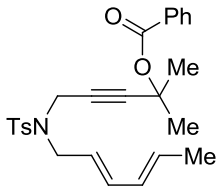
5-(*N*-((2*E*,4*E*)-hexa-2,4-dien-1-yl)-4-methylphenylsulfonamido)-2-methylpent-3-yn-2-yl acetate (168a)



Colourless solid, mp = 70-71 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.39 (s, 6H), 1.74 (d, 3H, J = 6.6 Hz), 1.95 (s, 3H), 2.41 (s, 3H), 3.83 (d, 2H, J = 7.0 Hz), 4.10 (s, 2H), 5.40 (dt, 1H, J = 7.0, 15.1 Hz), 5.65-5.73 (m, 1H), 6.02 (dd, 1H, J = 10.6, 15.0 Hz), 6.22 (dd, 1H, J = 10.6, 15.0 Hz), 7.29 (d, 2H, J = 8.2 Hz), 7.72 (d, 2H, J = 8.2 Hz); ^{13}C NMR ($CDCl_3$,

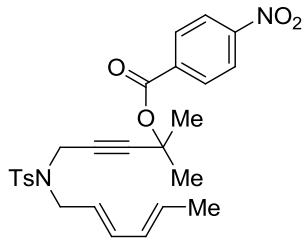
100 MHz): δ 18.1, 21.5, 21.8, 28.6, 36.0, 48.1, 71.4, 76.9, 86.8, 123.4, 127.8, 129.5, 130.6, 130.7, 135.6, 136.3, 143.2, 169.0; IR (NaCl, neat) *v*: 2985, 2305, 1738, 1422, 1265 cm^{-1}; HRMS (ESI) calcd. for $C_{21}H_{28}NO_4S$ (M^++H): 390.1739, found: 390.1741.

5-(*N*-((2*E*,4*E*)-hexa-2,4-dien-1-yl)-4-methylphenylsulfonamido)-2-methylpent-3-yn-2-yl benzoate (168b)



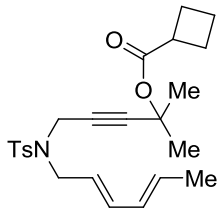
Colourless solid, mp = 89-92 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.53 (s, 6H), 1.66 (d, 3H, *J* = 7.2 Hz), 2.29 (s, 3H), 3.87 (d, 2H, *J* = 7.0 Hz), 4.12 (s, 2H), 5.35-5.56 (m, 2H), 5.97 (dd, 1H, *J* = 10.7, 14.7 Hz), 6.22 (dd, 1H, *J* = 10.5, 15.0 Hz), 7.17 (d, 2H, *J* = 8.01 Hz), 7.42 (d, 2H, *J* = 7.98 Hz), 7.53 (d, 2H, *J* = 7.38 Hz), 7.70 (d, 2H, *J* = 8.13 Hz), 7.95 (d, 2H, *J* = 7.4 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 18.0, 21.4, 28.8, 36.0, 48.2, 72.0, 77.1, 86.8, 123.3, 127.7, 128.3, 129.5, 130.5, 130.7, 130.9, 132.9, 135.8, 136.1, 143.2, 164.4; IR (NaCl, neat) *v*: 3053, 2986, 2351, 1737, 1599, 1422, 1265 cm^{-1}; HRMS (ESI) calcd. for $C_{26}H_{29}NO_4NaS$ (M^++Na): 474.1715, found: 474.1719.

5-(*N*-((2*E*,4*E*)-hexa-2,4-dien-1-yl)-4-methylphenylsulfonamido)-2-methylpent-3-yn-2-yl 4-nitrobenzoate (168c)



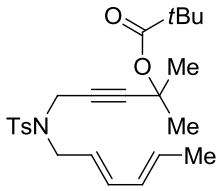
Colourless solid, mp = 86-87 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.56 (s, 6H), 1.68 (d, 3H, J = 6.2 Hz), 2.33 (s, 3H), 3.85 (d, 3H, J = 6.7 Hz), 4.11 (s, 2H), 5.39 (dt, 1H, J = 7.0, 15.1 Hz), 5.50-5.58 (m, 1H), 5.97 (dd, 1H, J = 10.8, 14.5 Hz), 6.19 (dd, 1H, J = 10.5, 15.0 Hz), 7.24 (d, 2H, J = 6.7 Hz), 7.71 (d, 2H, J = 8.1 Hz), 8.12 (d, 2H, J = 8.7 Hz), 8.26 (d, 2H, J = 8.7 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 18.0, 21.4, 28.7, 36.0, 48.2, 73.4, 78.0, 86.0, 123.4, 123.5, 127.7, 129.5, 130.5, 130.7, 135.6, 136.2, 143.2, 150.5, 162.5; IR (NaCl, neat) v: 2986, 2305, 1728, 1350, 1265 cm^{-1}; HRMS (ESI) calcd. for $C_{26}H_{28}N_2O_6NaS$ (M^++Na): 519.1566, found: 519.1567.

5-(*N*-((2*E*,4*E*)-hexa-2,4-dien-1-yl)-4-methylphenylsulfonamido)-2-methylpent-3-yn-2-yl cyclobutane carboxylate (168d)



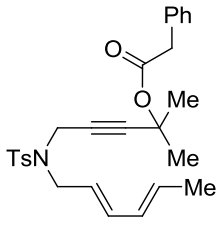
Yellow oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.35 (s, 6H), 1.71 (d, 3H, J = 6.6 Hz), 1.88-1.96 (m, 2H), 2.10-2.21 (m, 4H), 2.38 (s, 3H), 2.96-3.01 (m, 1H), 3.81 (d, 2H, J = 7.0 Hz), 4.08 (s, 2H), 5.38 (dt, 1H, J = 7.0, 15.1 Hz), 5.63-5.71 (m, 1H), 5.99 (dd, 1H, J = 11.3, 14.0 Hz), 6.21 (dd, 1H, J = 10.5, 14.9 Hz), 7.26 (d, 2H, J = 8.0 Hz), 7.68 (d, 2H, J = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 18.2, 21.4, 25.0, 28.6, 38.5, 48.0, 71.0, 76.6, 87.0, 123.4, 127.7, 129.5, 130.6, 130.6, 135.7, 136.3, 143.2, 173.4; IR (NaCl, neat) v: 3053, 2986, 2305, 1730, 1599, 1422, 1348, 1265 cm^{-1}; HRMS (ESI) calcd. for $C_{24}H_{31}NO_4NaS$ (M^++Na): 452.1872, found: 452.1872.

5-(*N*-((2*E*,4*E*)-hexa-2,4-dien-1-yl)-4-methylphenylsulfonamido)-2-methylpent-3-yn-2-yl pivalate (168e)



Colourless solid, mp = 79-80 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.12 (s, 9H), 1.37 (s, 6H), 1.73 (d, 3H, J = 6.6 Hz), 2.41 (s, 3H), 3.83 (d, 2H, J = 6.6 Hz), 4.08 (s, 2H), 5.40 (dt, 1H, J = 7.0, 15.1 Hz), 5.63-5.71 (m, 1H), 6.01 (dd, 1H, J = 10.8, 15.0 Hz), 6.22 (dd, 1H, J = 10.5, 15.1 Hz), 7.29 (d, 2H, J = 8.1 Hz), 7.72 (d, 2H, J = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 18.0, 21.4, 27.0, 28.4, 35.9, 38.9, 47.9, 70.9, 76.4, 87.0, 123.4, 127.6, 129.5, 130.5, 130.6, 135.6, 136.3, 143.2, 176.3; IR (NaCl, neat) v: 3053, 2986, 2305, 1728, 1599, 1422, 1346, 1265 cm^{-1}; HRMS (ESI) calcd. for $C_{24}H_{33}NO_4NaS$ (M^++Na): 454.2028, found: 454.2027.

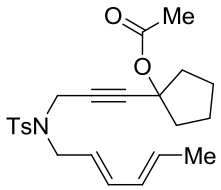
Benzyl (5-(*N*-((2*E*,4*E*)-hexa-2,4-dien-1-yl)-4-methylphenylsulfonamido)-2-methylpent-3-yn-2-yl) carbonate (168f)



Yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.42 (s, 6H), 1.73 (d, 3H, J = 6.6 Hz), 2.37 (s, 3H), 3.81 (d, 2H, J = 7.0 Hz), 4.09 (s, 2H), 5.10 (s, 2H), 5.41 (dt, 1H, J = 7.0, 15.1 Hz), 5.61-5.72 (m, 1H), 5.99-6.06 (m, 1H), 6.23 (dd, 1H, J = 10.5, 15.0 Hz), 7.24 (d, 2H, J = 8.1 Hz), 7.32-7.38 (m, 6H), 7.67 (d, 2H, J = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ

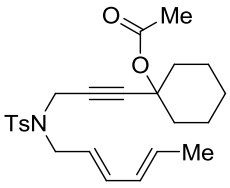
18.1, 21.5, 28.5, 35.9, 48.2, 69.2, 73.8, 77.4, 86.1, 123.3, 127.7, 127.8, 128.4, 128.4, 128.6, 128.6, 129.5, 130.5, 130.8, 135.2, 135.7, 136.0, 143.4, 152.7; IR (NaCl, neat) *v*: 3053, 2988, 2305, 1748, 1597, 1348, 1265 cm^{-1}; HRMS (ESI) calcd. for $C_{26}H_{29}NO_5SNa$ (M^++Na): 490.1644, found: 490.1656.

1-(3-(*N*-((2*E*,4*E*)-hexa-2,4-dien-1-yl)-4-methylphenylsulfonamido)prop-1-yn-1-yl)cyclopentyl acetate (168g)



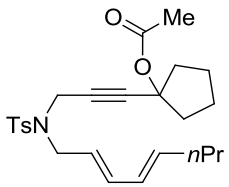
Colourless solid, mp = 80-82 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.24 (t, 1H, *J* = 6.6 Hz), 1.51-1.74 (m, 9H), 1.95-1.99 (m, 5H), 2.38 (s, 3H), 3.80 (d, 2H, *J* = 7.0 Hz), 4.08 (s, 2H), 5.37 (dt, 1H, *J* = 7.0, 15.0 Hz), 5.62-5.71 (m, 1H), 5.96-6.02 (m, 1H), 6.18 (dd, 1H, *J* = 10.5, 15.0 Hz), 7.26 (d, 2H, *J* = 8.0 Hz), 7.69 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 18.1, 21.5, 21.6, 23.2, 36.1, 40.1, 48.1, 77.3, 80.0, 86.4, 123.4, 127.7, 129.5, 130.5, 130.6, 135.6, 136.2, 143.2, 169.2; IR (NaCl, neat) *v*: 3053, 2986, 2304, 1736, 1422, 1265 cm^{-1}; HRMS (ESI) calcd. for $C_{23}H_{30}NO_4S$ (M^++H): 416.1896, found: 416.1896.

1-(3-(*N*-((2*E*,4*E*)-hexa-2,4-dien-1-yl)-4-methylphenylsulfonamido)prop-1-yn-1-yl)cyclohexyl acetate (168h)



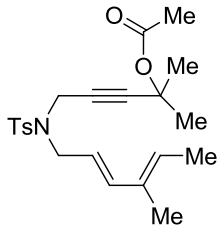
Colourless solid, mp = 86-88 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.20-1.36 (m, 5H), 1.43-1.44 (m, 2H), 1.59-1.63 (m, 1H), 1.69 (d, 2H, *J* = 6.6 Hz), 1.93 (s, 3H), 2.36 (s, 3H), 3.81 (d, 2H, *J* = 7.0 Hz), 4.10 (s, 2H), 5.37 (dd, 1H, *J* = 7.0, 15.1 Hz), 5.50-5.69 (m, 1H), 5.98 (dd, 1H, *J* = 11.9, 15.0 Hz), 6.18 (dd, 1H, *J* = 10.5, 15.1 Hz), 7.24 (d, 2H, *J* = 8.2 Hz), 7.67 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 18.1, 21.5, 21.8, 22.3, 25.0, 36.0, 36.6, 48.1, 74.8, 78.6, 85.7, 123.4, 127.6, 129.5, 130.5, 130.6, 135.6, 136.3, 143.2, 168.8; IR (NaCl, neat) *v*: 3053, 2986, 2305, 1736, 1645, 1422, 1265 cm^{-1}; HRMS (ESI) calcd. for $C_{21}H_{28}NO_4S$ (M^++H): 390.1739, found: 390.1742.

1-(3-(4-methyl-*N*-((2*E*,4*E*)-octa-2,4-dien-1-yl)phenylsulfonamido)prop-1-yn-1-yl)cyclopentyl acetate (168i)



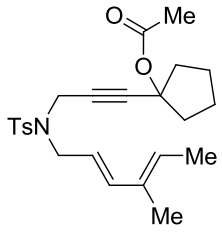
Yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.89 (t, 3H, *J* = 7.4 Hz), 1.35-1.44 (m, 2H), 1.54-1.66 (m, 5H), 1.72-1.78 (m, 2H), 1.94 (s, 3H), 1.95-2.07 (m, 3H), 2.41 (s, 3H), 3.82 (d, 2H, *J* = 6.8 Hz), 4.11 (s, 2H), 5.42 (dt, 1H, *J* = 6.8, 15.2 Hz), 5.67 (dd, 1H, *J* = 6.8, 15.2 Hz), 5.99 (dd, 1H, *J* = 10.4, 15.2 Hz), 6.21 (dd, 1H, *J* = 10.4, 15.2 Hz), 7.28 (d, 2H, *J* = 8.0 Hz), 7.72 (d, 2H, *J* = 8.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 13.7, 21.5, 21.6, 22.3, 23.2, 34.7, 36.1, 40.1, 48.2, 77.4, 80.0, 86.3, 123.7, 127.8, 129.3, 129.5, 135.7, 136.0, 136.4, 143.2, 169.2; IR (NaCl, neat) *v*: 3019, 2963, 2399, 1734, 1599, 1431, 1348, 1215 cm^{-1}; HRMS (ESI) calcd. for $C_{25}H_{33}NO_4SNa$ (M^++Na): 466.2028, found: 466.2011.

2-methyl-5-(4-methyl-*N*-((2*E*,4*E*)-4-methylhexa-2,4-dien-1-yl)phenylsulfonamido)pent-3-yn-2-yl acetate (168j)



Colourlesss solid, mp = 73-74 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.39 (s, 6H), 1.68-1.71 (m, 6H), 1.94 (s, 3H), 2.40 (s, 3H), 3.86 (d, 2H, J = 6.8 Hz), 4.10 (s, 2H), 3.82 (d, 2H, J = 6.8 Hz), 5.42 (dt, 1H, J = 7.0, 15.5 Hz), 5.55 (q, 1H, J = 6.8 Hz), 6.25 (d, 1H, J = 15.5 Hz), 7.28 (d, 2H, J = 8.0 Hz), 7.72 (d, 2H, J = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 12.0, 13.8, 21.5, 21.8, 28.7, 36.0, 48.5, 71.4, 76.9, 86.7, 119.1, 127.8, 128.0, 129.5, 133.8, 136.4, 140.1, 143.2, 169.0; IR (NaCl, neat) v: 3022, 2920, 2361, 1740, 1348, 1246, 1161 cm^{-1}; HRMS (ESI) calcd. for $C_{22}H_{29}NO_4SNa$ (M^++Na): 426.1715, found: 426.1721.

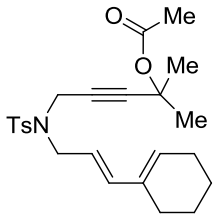
1-(3-(4-methyl-*N*-((2*E*,4*E*)-4-methylhexa-2,4-dien-1-yl)phenylsulfonamido)prop-1-yn-1-yl)cyclopentyl acetate (168k)



Colourlesss solid, mp = 85-86 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.55-1.75 (m, 12H), 1.93-1.99 (m, 5H), 2.39 (s, 3H), 3.85 (d, 2H, J = 6.9 Hz), 4.10 (s, 2H), 5.36 (dt, 1H, J = 6.9, 15.5 Hz), 5.51 (q, 1H, J = 6.8 Hz), 7.27 (d, 2H, J = 8.0 Hz), 7.70 (d, 2H, J = 8.1 Hz);

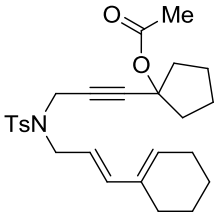
^{13}C NMR ($CDCl_3$, 100 MHz): δ 12.0, 13.8, 21.5, 21.6, 23.2, 36.0, 40.1, 48.5, 77.4, 80.0, 86.3, 119.1, 127.7, 127.9, 129.5, 133.8, 136.4, 140.1, 143.2, 169.2; IR (NaCl, neat) *v*: 3023, 2961, 1740, 1348, 1161, 1094 cm^{-1}; HRMS (ESI) calcd. for $C_{24}H_{31}NO_4SNa$ (M^++Na): 452.1871, found: 452.1877.

(*E*)-5-(*N*-(3-(cyclohex-1-en-1-yl)allyl)-4-methylphenylsulfonamido)-2-methylpent-3-yn-2-yl acetate (168l)



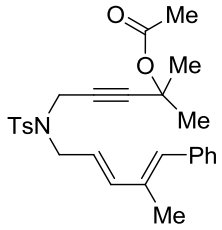
Colourlesss solid, mp = 90-92 °C; ^{1}H NMR ($CDCl_3$, 400MHz): δ 1.36 (s, 6H), 1.55-1.62 (m, 4H), 1.92 (s, 3H), 1.93-2.08 (m, 4H), 2.38 (s, 3H), 3.84 (d, 2H, *J* = 6.8 Hz), 4.08 (s, 2H), 5.34 (dt, 1H, *J* = 7.4, 15.6 Hz), 5.71 (s, 1H), 6.20 (d, 1H, *J* = 15.6 Hz), 7.27 (d, 2H, *J* = 7.8 Hz), 7.70 (d, 2H, *J* = 8.1 Hz); ^{13}C NMR ($CDCl_3$, 100MHz): 21.5, 21.8, 22.3, 22.4, 24.4, 25.8, 28.6, 36.0, 48.5, 71.4, 76.9, 86.8, 118.5, 127.7, 129.5, 130.5, 135.0, 136.3, 138.8, 143.2, 168.9; IR (NaCl, neat) *v*: 2934, 1738, 1346, 1206, 1136 cm^{-1}; HRMS (ESI) calcd. for $C_{24}H_{31}NO_4SNa$ (M^++Na): 452.1871, found: 454.1880.

(*E*)-1-(3-(*N*-(3-(cyclohex-1-en-1-yl)allyl)-4-methylphenylsulfonamido)prop-1-yn-1-yl)cyclopentyl acetate (168m)



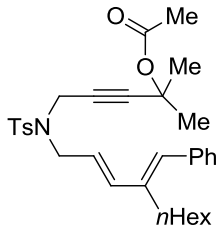
Colourlesss solid, mp = 96-98 °C; ^{1}H NMR ($CDCl_3$, 400MHz): δ 1.56-1.76 (m, 10H), 1.95-2.09 (m, 9H), 2.40 (s, 3H), 3.84 (d, 2H, *J* = 6.8 Hz), 4.11 (s, 2H), 5.34 (dt, 1H, *J* = 6.8, 15.6 Hz), 5.72 (s, 1H), 6.20 (d, 1H, *J* = 15.6 Hz), 7.28 (d, 2H, *J* = 8.0 Hz), 7.70 (d, 2H, *J* = 8.0 Hz); ^{13}C NMR ($CDCl_3$, 100MHz): 21.5, 21.6, 22.3, 22.4, 24.4, 25.8, 36.1, 48.5, 77.1, 78.0, 86.3, 118.5, 127.7, 129.5, 130.5, 135.0, 136.4, 138.8, 143.2, 169.2; IR (NaCl, neat) *v*: 2930, 1734, 1346, 1215, 1161 cm^{-1}; HRMS (ESI) calcd. for $C_{26}H_{33}NO_4SNa$ (M^++Na): 478.2028, found: 478.2022.

2-methyl-5-(4-methyl-*N*-((2*E*,4*E*)-4-methyl-5-phenylpenta-2,4-dien-1 yl)phenylsulfonamido) pent-3-yn-2-yl acetate (168n)



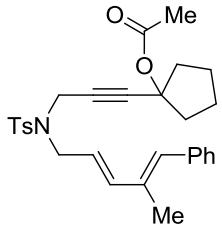
Colourless solid, mp = 103-105 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): *δ* 1.42 (s, 6H), 1.95 (s, 3H), 1.97 (s, 3H), 2.42 (s, 3H), 3.96 (d, 2H, *J* = 6.8 Hz), 4.2 (s, 2H), 5.63 (dt, 1H, *J* = 7.2, 15.2 Hz), 6.47 (d, 1H, *J* = 15.6 Hz), 6.51 (s, 1H), 7.20-7.36 (m, 7H), 7.76 (d, 2H, *J* = 8.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): *δ* 13.9, 21.5, 21.9, 28.7, 36.2, 48.5, 71.4, 76.9, 86.9, 122.1, 126.8, 127.8, 128.2, 129.2, 129.5, 132.2, 134.9, 136.4, 137.5, 140.3, 143.3, 169.0; IR (NaCl, neat) *v*: 3017, 2398, 1740, 1491, 1346, 1263 cm^{-1}; HRMS (ESI) calcd. for $C_{27}H_{31}NO_4SNa$ (M^++Na): 488.1872, found: 488.1870.

5-(*N*-((2*E*,4*E*)-4-benzylidenedec-2-enyl)-4-methylphenylsulfonamido)-2-methylpent-3-yn-2-yl acetate (168o)



Pale-yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.89 (brs, 3H), 1.29-1.49 (m, 14H), 1.96 (s, 3H), 2.38-2.42 (m, 5H), 3.96 (d, 2H, J = 6.2 Hz), 4.15 (s, 2H), 5.60-5.64 (m, 1H), 6.35 (d, 1H, J = 15.5 Hz), 6.45 (s, 1H), 7.24-7.32 (m, 7H), 7.76 (d, 2H, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.1, 21.5, 21.9, 22.7, 27.6, 28.7, 29.1, 29.6, 31.6, 36.1, 48.5, 71.4, 76.8, 87.0, 121.6, 126.8, 127.8, 128.3, 128.7, 129.6, 131.8, 136.3, 137.5, 139.6, 139.9, 143.3, 169.0; IR (NaCl, neat) v: 2928, 1742, 1348, 1244, 1161 cm^{-1}; HRMS (ESI) calcd. for $C_{32}H_{41}NO_4SNa$ (M^++Na): 558.2654, found: 558.2661.

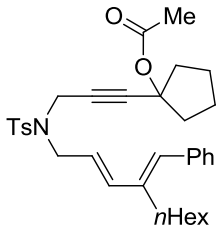
1-(3-(4-methyl-*N*-((2*E*,4*E*)-4-methyl-5-phenylpenta-2,4-dien-1-yl)phenylsulfonamido) prop-1-yn-1-yl)cyclopentyl acetate (168p)



Colourless solid, mp = 137-139 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.59-1.66 (m, 4H), 1.75-1.80 (m, 2H), 1.91 (s, 3H), 1.95 (s, 3H), 1.97-2.04 (m, 2H), 2.42 (s, 3H), 3.95 (d, 2H, J = 6.8 Hz), 4.17 (s, 2H), 5.63 (dt, 1H, J = 6.8, 15.6 Hz), 6.45 (d, 1H, J = 15.6 Hz), 6.50 (s, 1H), 7.21-7.36 (m, 7H), 7.75 (d, 2H, J = 8.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 13.9,

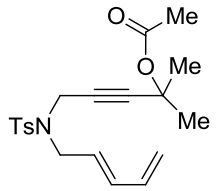
21.5, 21.7, 23.3, 36.3, 40.1, 48.5, 77.6, 80.0, 86.5, 122.1, 126.7, 127.8, 128.2, 129.2, 129.5, 132.2, 134.9, 136.4, 137.5, 140.2, 143.3, 169.3; IR (NaCl, neat) *v*: 3019, 2963, 1736, 1431, 1346, 1305 cm^{-1}; HRMS (ESI) calcd. for $C_{29}H_{33}NO_4SNa$ (M^++Na): 514.2028, found: 514.2017.

1-(3-(*N*-((2*E*,4*E*)-4-benzylidenedec-2-en-1-yl)-4-methylphenylsulfonamido)prop-1-yn-1-yl) cyclo-pentyl acetate (168q)



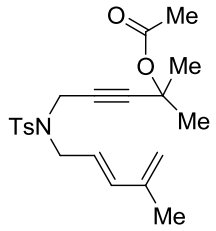
Pale-yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.89 (t, 3H, *J* = 6.6 Hz), 1.29-1.37 (m, 6H), 1.45-1.53 (m, 2H), 1.57-1.69 (m, 4H), 1.75-1.82 (m, 2H), 1.97-2.06 (m, 5H), 2.35-2.42 (m, 5H), 3.96 (d, 2H, *J* = 7.0 Hz), 4.16 (s, 2H), 5.62 (dt, 1H, *J* = 7.0, 15.6 Hz), 6.34 (d, 1H, *J* = 15.6 Hz), 6.45 (s, 1H), 7.20-7.35 (m, 7H), 7.75 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.1, 21.5, 21.7, 22.7, 23.3, 27.5, 29.1, 29.7, 31.6, 36.2, 40.1, 48.5, 77.3, 80.0, 86.5, 121.6, 126.8, 127.8, 128.3, 128.7, 129.6, 131.8, 136.3, 137.5, 139.6, 139.9, 143.3, 169.2; IR (NaCl, neat) *v*: 3022, 2928, 1740, 1445, 1350, 1242, 1161cm^{-1}; HRMS (ESI) calcd. for $C_{34}H_{43}NO_4SNa$ (M^++Na): 584.2810, found: 584.2816.

(*E*)-2-methyl-5-(4-methyl-*N*-(penta-2,4-dien-1-yl)phenylsulfonamido)pent-3-yn-2-yl acetate (168r)



Colourless solid, mp = 74-76 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.39 (s, 6H), 1.94 (m, 3H), 2.41 (s, 3H), 3.86 (d, 2H, *J* = 6.9 Hz), 4.10 (s, 2H), 5.08-5.24 (m, 2H), 5.52-5.62 (m, 1H), 6.22-6.37 (m, 2H), 7.29 (d, 2H, *J* = 8.1 Hz), 7.72 (d, 2H, *J* = 8.1 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 21.5, 21.8, 28.6, 36.2, 48.0, 71.4, 76.8, 86.9, 118.2, 127.0, 127.8, 129.5, 135.7, 136.0, 136.2, 143.3, 169.0; IR (NaCl, neat) *v*: 3019, 2399, 1734, 1600, 1425, 1348, 1265 cm^{-}1; HRMS (ESI) calcd. for $C_{20}H_{25}NO_4SNa$ (M^{+}+Na): 398.1402, found: 398.1395.

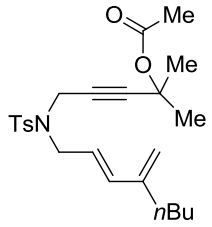
(*E*)-2-methyl-5-(4-methyl-*N*-(4-methylpenta-2,4-dien-1-yl)phenylsulfonamido)pent-3-yn-2-yl acetate (168s)



Colourlesss solid, mp = 82-84 °C; ^{1}H NMR ($CDCl_3$, 400MHz): δ 1.37 (m, 6H), 1.38 (s, 3H), 1.93 (s, 3H), 2.39 (s, 3H), 3.88 (d, 2H, *J* = 6.9 Hz), 4.09 (s, 2H), 4.94 (s, 1H), 4.96 (s, 1H), 5.49 (dt, 1H, *J* = 6.9, 15.6 Hz), 6.34 (d, 1H, *J* = 15.6 Hz), 7.28 (d, 2H, *J* = 8.1 Hz), 7.71 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100MHz): 18.5, 21.5, 21.8, 28.6, 36.2, 48.2, 71.4, 76.8, 86.9, 117.3, 122.9, 127.7, 129.5, 136.3, 137.8, 141.2, 143.3, 169.0; IR (NaCl,

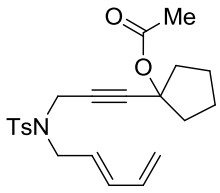
neat) *v*: 3021, 1734, 1348, 1215, 1161 cm^{-1}; HRMS (ESI) calcd. for $C_{21}H_{27}NO_4SNa$ (M^++Na): 412.1558, found: 412.1553.

(*E*)-2-methyl-5-(4-methyl-*N*-(4-methyleneoct-2-en-1-yl)phenylsulfonamido)pent-3-yn-2-yl acetate (168t)



Colourlesss oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.90 (t, 3H, *J* = 7.2 Hz), 1.28-1.43 (m, 10H), 1.94 (s, 3H), 2.11-2.15 (m, 2H), 2.41 (s, 3H), 3.88 (d, 2H, *J* = 6.9 Hz), 4.10 (s, 2H), 4.96 (s, 2H), 5.63 (dt, 1H, *J* = 6.9, 15.7 Hz), 6.26 (d, 1H, *J* = 15.7 Hz), 7.28 (d, 2H, *J* = 8.0 Hz), 7.72 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.0, 21.5, 21.8, 22.6, 28.6, 30.3, 31.7, 36.1, 48.4, 71.4, 76.8, 86.9, 116.1, 122.0, 127.8, 129.5, 136.3, 137.5, 143.3, 145.5, 169.0; IR (NaCl, neat) *v*: 2933, 2860, 1741, 1355, 1163 cm^{-1}; HRMS (ESI) calcd. for $C_{24}H_{33}NO_4SNa$ (M^++Na): 454.2028, found: 454.2021.

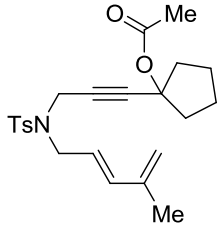
(*E*)-1-(3-(4-methyl-*N*-(penta-2,4-dien-1-yl)phenylsulfonamido)prop-1-yn-1-yl)cyclopentyl acetate (168u)



Colourless solid; mp = 83-85 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.58-1.80 (m, 6H), 1.92-2.02 (m, 5H), 2.40 (s, 3H), 3.86 (d, 2H, *J* = 6.6 Hz), 4.11 (s, 2H), 5.08-5.22 (m, 2H),

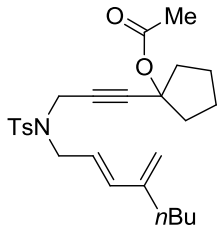
5.57 (dt, 1H, *J* = 6.9, 14.1 Hz), 6.21-6.36 (m, 2H), 7.29 (d, 2H, *J* = 8.1 Hz), 7.71 (d, 2H, *J* = 8.4 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 21.5, 21.6, 23.2, 36.3, 40.1, 48.0, 77.3, 80.0, 86.5, 118.2, 127.0, 127.7, 129.5, 135.7, 136.0, 136.3, 143.3, 169.2; IR (NaCl, neat) *v*: 3019, 2399, 1734, 1599, 1431, 1348, 1215 cm^{-1}; HRMS (ESI) calcd. for $C_{22}H_{27}NO_4SNa$ (M^++Na): 424.1559, found: 424.1552.

(*E*)-1-(3-(4-methyl-*N*-(4-methylpenta-2,4-dien-1-yl)phenylsulfonamido)prop-1-yn-1-yl)cyclopentyl acetate (168v)



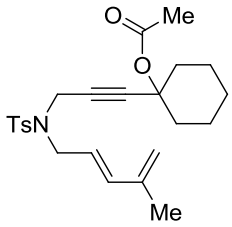
Colourlesss solid; mp = 102-104 °C; ^{1}H NMR ($CDCl_3$, 400MHz): δ 1.53-1.67 (m, 4H), 1.71-1.79 (m, 5H), 1.94-2.01 (m, 5H), 2.40 (m, 3H), 3.87 (d, 2H, *J* = 6.9 Hz), 4.11 (s, 2H), 4.94 (s, 1H), 4.96 (s, 1H), 5.49 (dt, 1H, *J* = 6.9, 15.6 Hz), 6.32 (d, 1H, *J* = 15.6 Hz), 7.28 (d, 2H, *J* = 8.1 Hz), 7.71 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100MHz): 18.5, 21.5, 21.6, 23.2, 36.3, 40.1, 48.2, 77.3, 80.0, 86.5, 117.3, 122.9, 127.7, 129.5, 136.3, 137.8, 141.2, 143.3, 169.2; IR (NaCl, neat) *v*: 3021, 1732, 1611, 1599, 1435, 1217 cm^{-1}; HRMS (ESI) calcd. for $C_{23}H_{29}NO_4SNa$ (M^++Na): 438.1715, found: 438.1715.

(*E*)-1-(3-(4-methyl-*N*-(4-methyleneoct-2-en-1-yl)phenylsulfonamido)prop-1-yn-1-yl)cyclopentyl acetate (168w)



Pale-yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.88 (t, 3H, J = 7.2 Hz), 1.23-1.42 (m, 4H), 1.52-1.64 (m, 4H), 1.70-1.76 (m, 2H), 1.92-1.99 (m, 5H), 2.09-2.12 (m, 2H), 2.38 (s, 3H), 3.86 (d, 2H, J = 6.9 Hz), 4.09 (s, 2H), 4.94 (s, 2H), 5.63 (dt, 1H, J = 6.9, 15.7 Hz), 6.23 (d, 1H, J = 15.8 Hz), 7.27 (d, 2H, J = 8.1 Hz), 7.70 (d, 2H, J = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 13.9, 21.5, 21.6, 22.6, 23.2, 30.3, 31.7, 36.2, 48.4, 77.2, 79.9, 86.5, 116.1, 122.0, 127.7, 129.5, 136.3, 137.4, 143.3, 145.5, 169.2; IR (NaCl, neat) v: 2957, 2932, 2872, 1742, 1450, 1350, 1242, 1163 cm^{-1}; HRMS (ESI) calcd. for $C_{26}H_{35}NO_4SNa$ (M^++Na): 480.2184, found: 480.2177.

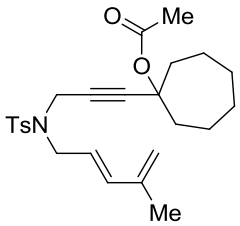
(*E*)-1-(3-(4-methyl-*N*-(4-methylpenta-2,4-dien-1-yl)phenylsulfonamido)prop-1-yn-1-yl)cyclohexyl acetate (168x)



Colourlesss solid; mp = 104-106 °C; ^{1}H NMR ($CDCl_3$, 400MHz): δ 1.24-1.48 (m, 6H), 1.63-1.78 (m, 7H), 1.95 (s, 3H), 2.39 (m, 3H), 3.90 (d, 2H, J = 6.9 Hz), 4.15 (s, 2H), 4.94 (s, 1H), 4.97 (s, 1H), 5.50 (dt, 1H, J = 6.9, 15.6 Hz), 6.33 (d, 1H, J = 15.6 Hz), 7.28 (d,

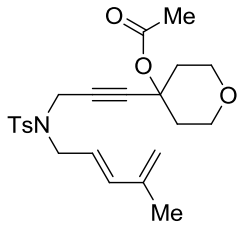
2H, *J* = 8.2 Hz), 7.72 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100MHz): 18.5, 21.5, 21.8, 22.3, 25.0, 36.2, 36.7, 48.2, 74.9, 78.7, 85.8, 117.4, 122.9, 127.7, 129.6, 136.4, 137.8, 141.2, 143.2, 168.8; IR (NaCl, neat) *v*: 3021, 2938, 1927, 1738, 1233, 1217, 1161 cm^{-1}; HRMS (ESI) calcd. for $C_{24}H_{31}NO_4SNa$ (M^++Na): 452.1872, found: 452.1880.

(*E*)-1-(3-(4-methyl-*N*-(4-methylpenta-2,4-dien-1-yl)phenylsulfonamido)prop-1-yn-1-yl)cycloheptyl acetate (168y)



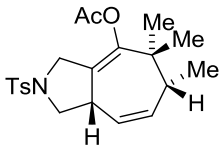
Colourlesss solid; mp = 78-80 °C; ^{1}H NMR ($CDCl_3$, 400MHz): δ 1.35-1.49 (m, 8H), 1.78 (s, 3H), 1.87-1.88 (m, 4H), 1.94 (s, 3H), 2.40 (m, 3H), 3.89 (d, 2H, *J* = 6.8 Hz), 4.13 (s, 2H), 4.94 (s, 1H), 4.96 (s, 1H), 5.50 (dt, 1H, *J* = 6.8, 15.6 Hz), 6.33 (d, 1H, *J* = 15.6 Hz), 7.28 (d, 2H, *J* = 7.9 Hz), 7.71 (d, 2H, *J* = 8.0 Hz); ^{13}C NMR ($CDCl_3$, 100MHz): 18.5, 21.5, 21.9, 22.0, 28.3, 36.2, 39.9, 48.1, 77.8, 78.2, 87.1, 117.3, 123.0, 127.7, 129.6, 136.4, 137.8, 141.2, 143.2, 168.9; IR (NaCl, neat) *v*: 3021, 2932, 1734, 1348, 1246, 1159 cm^{-1}; HRMS (ESI) calcd. for $C_{25}H_{33}NO_4SNa$ (M^++Na): 466.2028, found: 466.2029.

(*E*)-4-(3-(4-methyl-*N*-(4-methylpenta-2,4-dien-1-yl)phenylsulfonamido)prop-1-yn-1-yl)tetrahydro-2H-pyran-4-yl acetate (168z)



Colourlesss solid; mp = 83-84 °C; ^{1}H NMR ($CDCl_3$, 400MHz): δ 1.75 (s, 3H), 1.77-1.89 (m, 4H), 1.95 (s, 3H), 2.37 (s, 3H), 3.34-3.39 (m, 2H), 3.61-3.67 (m, 2H), 3.88 (d, 2H, *J* = 6.8 Hz), 4.13 (s, 2H), 4.92 (s, 1H), 4.95 (s, 1H), 5.47 (dt, 1H, *J* = 6.9, 15.6 Hz), 6.29 (d, 1H, *J* = 15.6 Hz), 7.26 (d, 2H, *J* = 8.0 Hz), 7.69 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100MHz): 18.4, 21.4, 21.7, 36.1, 37.1, 48.3, 64.0, 71.9, 79.7, 84.4, 117.5, 122.8, 127.6, 129.6, 136.3, 137.8, 141.1, 143.4, 168.7; IR (NaCl, neat) *v*: 2968, 1740, 1435, 1348, 1233, 1161 cm^{-1}; HRMS (ESI) calcd. for $C_{23}H_{29}NO_5SNa$ (M^++Na): 454.1664, found: 454.1664.

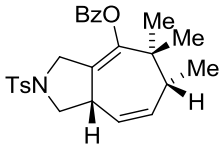
(6*R,8a*S**)-5,5,6-trimethyl-2-tosyl-1,2,3,5,6,8a-hexahydrocyclohepta[*c*]pyrrol-4-yl acetate (169a)**



Colourless solid, mp = 89-91 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): *δ* 0.84 (s, 3H), 0.99 (d, 3H, *J* = 7.0 Hz), 1.02 (s, 3H), 2.12 (s, 3H), 2.40-2.48 (m, 4H), 2.81 (t, 1H, *J* = 9.4 Hz), 3.54 (d, 1H, *J* = 14.4 Hz), 3.63 (t, 1H, *J* = 9.2 Hz), 3.73 (t, 1H, *J* = 9.0 Hz), 3.86 (d, 2H, *J* = 14.1 Hz), 5.40-5.45 (m, 1H), 5.50 (d, 2H, *J* = 10.7 Hz), 7.32 (d, 2H, *J* = 8.0 Hz), 7.67 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): *δ* 15.7, 20.1, 20.6, 21.5, 24.7, 38.6,

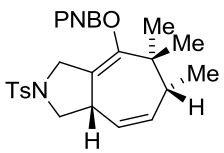
39.8, 41.0, 51.0, 54.0, 77.3, 126.2, 128.9, 132.4, 137.1, 143.9, 147.5, 168.0; IR (NaCl, neat) *v*: 3053, 2986, 1738, 1422, 1346, 1265 cm^{-1}; HRMS (ESI) calcd. for $C_{21}H_{28}NO_4S$ (M^++H): 390.1739, found: 390.1742.

(6*R,8a*S**)-5,5,6-trimethyl-2-tosyl-1,2,3,5,6,8a-hexahydrocyclohepta[*c*]pyrrol-4-yl benzoate (169b)**



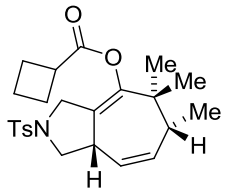
Colourless solid, mp = 125-126 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.92 (s, 3H), 1.04 (d, 3H, *J* = 7.0 Hz), 1.10 (s, 3H), 2.43 (s, 3H), 2.57 (t, 2H, *J* = 6.4 Hz), 2.86 (bs, 1H), 3.55-3.66 (m, 1H), 3.72-3.77 (m, 2H), 3.92-3.97 (m, 1H), 5.46-5.50 (m, 1H), 5.57 (d, 1H, *J* = 9.7 Hz), 7.31 (d, 2H, *J* = 8.0 Hz), 7.49 (t, 2H, *J* = 7.9 Hz), 7.61-7.66 (m, 3H), 8.07 (d, 2H, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 15.6, 21.6, 24.3, 24.8, 38.7, 40.0, 41.4, 51.2, 54.1, 126.6, 128.0, 128.6, 129.2, 129.8, 130.1, 132.3, 133.6, 137.3, 143.8, 147.5, 163.2; IR (NaCl, neat) *v*: 3053, 2986, 2305, 1732, 1599, 1422, 1348, 1265 cm^{-1}; HRMS (ESI) calcd. for $C_{26}H_{30}NO_4S$ (M^++H): 452.1896, found: 452.1896.

(6*R,8a*S**)-5,5,6-trimethyl-2-tosyl-1,2,3,5,6,8a-hexahydrocyclohepta[*c*]pyrrol-4-yl 4-nitrobenzoate (169c)**



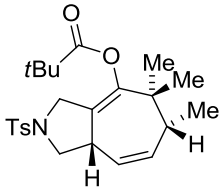
Colourless solid, mp = 175-177 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.93 (s, 3H), 1.06 (d, 3H, J = 6.8 Hz), 1.10 (s, 3H), 2.58 (t, 1H, J = 6.4 Hz), 2.87 (bs, 1H), 3.58 (bs, 1H), 3.77 (t, 2H, J = 8.8 Hz), 3.92 (d, 1H, J = 12.1 Hz), 5.50-5.60 (m, 2H), 7.33 (d, 2H, J = 7.8 Hz), 7.65 (d, 2H, J = 7.8 Hz), 8.23 (d, 2H, J = 8.5 Hz), 8.35 (d, 2H, J = 8.5 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 15.6, 21.6, 24.8, 38.7, 39.7, 41.4, 51.1, 54.0, 123.8, 127.2, 127.3, 127.9, 129.6, 129.8, 131.1, 131.2, 132.3, 134.5, 137.3, 144.0, 147.5, 150.9, 161.8; IR (NaCl, neat) v: 3053, 2986, 1737, 1531, 1348, 1265 cm^{-1}; HRMS (ESI) calcd. for $C_{26}H_{28}N_2O_6SNa$ (M^++Na): 519.1566, found: 519.1564.

(6*R,8a*S**)-5,5,6-trimethyl-2-tosyl-1,2,3,5,6,8a-hexahydrocyclohepta[*c*]pyrrol-4-yl cyclobutane carboxylate (169d)**



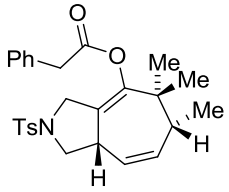
Colourless solid; mp = 125-127 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.82 (s, 3H), 0.99 (d, 2H, J = 7.0 Hz), 1.02 (s, 4H), 1.90-2.08 (m, 2H), 2.22-2.34 (m, 4H), 2.42 (s, 3H), 2.47 (t, 1H, J = 6.7 Hz), 2.80 (t, 1H, J = 9.6 Hz), 3.21 (m, 1H), 3.50 (d, 1H, J = 13.3 Hz), 3.63 (t, 1H, J = 8.9 Hz), 3.74 (t, 1H, J = 8.9 Hz), 3.83-3.90 (m, 1H), 5.40-5.45 (m, 1H), 5.50 (d, 1H, J = 10.4 Hz), 7.32 (d, 2H, J = 8.0 Hz), 7.66 (d, 2H, J = 8.6 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 15.7, 18.6, 21.6, 24.7, 25.4, 37.9, 38.6, 39.9, 41.1, 51.0, 54.0, 125.9, 127.9, 129.8, 132.4, 137.2, 143.9, 147.4, 172.3; IR (NaCl, neat) v: 3053, 2986, 2305, 1741, 1599, 1422, 1346, 1265 cm^{-1}; HRMS (ESI) calcd. for $C_{24}H_{31}NO_4SNa$ (M^++Na): 452.1872, found: 452.1874.

(6*R,8a*S**)-5,5,6-trimethyl-2-tosyl-1,2,3,5,6,8a-hexahydrocyclohepta[*c*]pyrrol-4-yl pivalate (169e)**



Yellow solid, mp = 115-118 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.82 (s, 9H), 0.99-1.02 (m, 6H), 2.43 (s, 3H), 2.49 (t, 1H, J = 6.5 Hz), 2.78 (bs, 1H), 3.65-3.84 (m, 4H), 5.41-5.46 (m, 1H), 5.51 (d, 2H, J = 10.0 Hz), 7.32 (d, 2H, J = 8.0 Hz), 7.65 (d, 2H, J = 8.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 15.6, 21.6, 24.6, 27.0, 27.0, 27.2, 38.6, 39.2, 39.7, 41.3, 51.0, 54.0, 125.7, 127.7, 127.9, 129.7, 132.1, 137.2, 143.9, 147.5, 175.3; IR (NaCl, neat) v: 3053, 2984, 1744, 1599, 1422, 1348, 1265 cm^{-1}; HRMS (ESI) calcd. for $C_{24}H_{23}NO_4SNa$ (M^++Na): 454.2028, found: 454.2029.

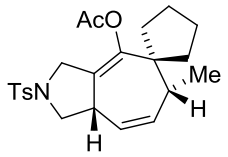
Benzyl ((6*R,8a*S**)-5,5,6-trimethyl-2-tosyl-1,2,3,5,6,8a-hexahydrocyclohepta[*c*]pyrrol-4-yl) carbonate (169f)**



Yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.85 (s, 3H), 0.98 (d, 3H, J = 6.9 Hz), 1.05 (s, 3H), 2.42 (s, 3H), 2.44-2.47 (m, 1H), 2.74 (t, 1H, J = 9.8 Hz), 3.52-3.56 (m, 1H), 3.65 (t, 1H, J = 9.3 Hz), 3.77 (t, 1H, J = 8.9 Hz), 3.94-4.03 (m, 1H), 5.16-5.23 (m, 2H), 5.41-5.50 (m, 2H), 7.29 (d, 2H, J = 8.0 Hz), 7.32-7.45 (m, 5H), 7.61 (d, 2H, J = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 15.6, 21.6, 24.4, 38.6, 41.2, 50.7, 53.9, 70.2, 127.1, 128.0, 128.2,

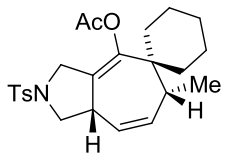
128.7, 129.7, 132.2, 135.1, 137.3, 143.9, 148.1, 152.6; IR (NaCl, neat) *v*: 3053, 2986, 23005, 1759, 1422, 1265 cm^{-1}; HRMS (ESI) calcd. for $C_{26}H_{30}NO_5S$ (M^++H): 468.1845, found: 468.1851.

(6*R,8a*S**)-6-methyl-2-tosyl-2,3,6,8a-tetrahydro-1*H*-spiro[cyclohepta[*c*]pyrrole-5,1'-cyclopentan]-4-yl acetate (169g)**



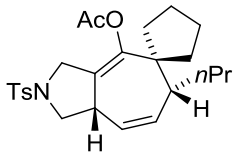
Colourless solid; mp = 167-168 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.96 (d, 3H, *J* = 6.8 Hz), 1.24-1.36 (m, 2H), 1.49-1.72 (m, 5H), 1.84-1.89 (m, 1H), 2.13 (s, 1H), 2.17 (s, 1H), 2.42 (s, 3H), 2.77 (t, 1H, *J* = 9.7 Hz), 3.52-3.61 (m, 2H), 3.74 (t, 1H, *J* = 8.7 Hz), 3.89 (d, 1H, *J* = 14.3 Hz), 5.28-5.30 (m, 1H), 5.50-5.54 (m, 1H), 7.32 (d, 2H, *J* = 7.9 Hz), 7.68 (d, 2H, *J* = 8.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 17.7, 20.6, 21.5, 25.3, 29.7, 36.5, 39.7, 51.1, 52.6, 54.6, 125.7, 127.9, 129.8, 132.6, 135.9, 143.9, 147.4, 167.7; IR (NaCl, neat) *v*: 3053, 2986, 1748, 1422, 1265 cm^{-1}; HRMS (ESI) calcd. for $C_{23}H_{30}NO_4S$ (M^++H): 416.1896, found: 416.1894.

(6*R,8a*S**)-6-methyl-2-tosyl-2,3,6,8a-tetrahydro-1*H*-spiro[cyclohepta[*c*]pyrrole-5,1'-cyclohexan]-4-yl acetate (169h)**



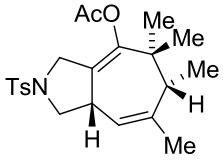
Yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.90 (d, 3H, J = 6.8 Hz), 1.37-1.75 (m, 10H), 2.13 (s, 3H), 2.38-2.43 (m, 4H), 2.71 (t, 1H, J = 9.9 Hz), 3.37-3.42 (m, 1H), 3.66 (d, 1H, J = 14.4 Hz), 3.78 (t, 1H, J = 8.6 Hz), 3.95 (d, 1H, J = 14.4 Hz), 5.20 (dd, 1H, J = 2.2, 12.0 Hz), 5.57-5.62 (m, 1H), 7.33 (d, 2H, J = 8.0 Hz), 7.69 (d, 2H, J = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 16.8, 20.6, 21.6, 22.0, 25.6, 40.8, 43.8, 51.1, 54.8, 121.7, 125.8, 127.8, 129.8, 133.0, 134.4, 143.8, 147.2, 167.9; IR (NaCl, neat) v: 3053, 2986, 1755, 1422, 1346, 1265 cm^{-1}; HRMS (ESI) calcd. for $C_{24}H_{23}NO_4SNa$ (M^++Na): 452.1872, found: 452.1871.

(6*R,8a*S**)-6-propyl-2-tosyl-2,3,6,8a-tetrahydro-1*H*-spiro[cyclohepta[*c*]pyrrole-5,1'-cyclopentan]-4-yl acetate (169i)**



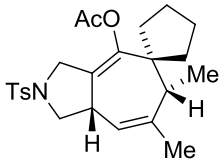
Yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.86 (t, 3H, J = 7.4 Hz), 1.21-1.69 (m, 7H), 1.74-1.77 (m, 1H), 1.91-1.96 (m, 2H), 2.01 (s, 2H), 2.12-2.14 (m, 4H), 2.43 (s, 3H), 3.09 (dd, 1H, J = 3.6, 9.6 Hz), 3.26 (d, 1H, J = 9.2 Hz), 3.58 (d, 1H, J = 9.2 Hz), 3.74 (d, 1H, J = 9.2 Hz), 4.94-5.00 (m, 1H), 5.40-5.50 (m, 1H), 7.32 (d, 2H, J = 8.0 Hz), 7.67-7.70 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 13.6, 20.5, 21.5, 22.7, 25.8, 26.8, 29.2, 29.2, 29.3, 30.1, 34.6, 49.7, 52.9, 127.0, 127.5, 129.6, 131.2, 133.8, 135.6, 136.6, 143.4, 169.1; IR (NaCl, neat) v: 3020, 2959, 1751, 1458, 1346, 1215 cm^{-1}; HRMS (ESI) calcd. for $C_{25}H_{33}NO_4SNa$ (M^++Na): 466.2028, found: 466.2014.

(6*R,8*aS**)-5,5,6,7-tetramethyl-2-tosyl-1,2,3,5,6,8a-hexahydrocyclohepta[c]pyrrol-4-yl acetate (169j)**



Colourless solid, mp = 130-132 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.83-1.15 (m, 9 H), 1.65 (s, 3H), 2.12 (s, 3H), 2.42 (s, 3H), 2.79 (brs, 1H), 3.53-3.73 (m, 3H), 3.88 (brs, 1H), 5.02-5.40 (m, 1H), 7.32 (d, 2H, *J* = 8.0 Hz), 7.68 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 20.5, 21.5, 28.3, 41.1, 50.9, 127.3, 127.9, 129.5, 129.8, 143.8; IR (NaCl, neat) *v*: 2974, 2868, 1748, 1346, 1215 cm^{-1}; HRMS (ESI) calcd. for $C_{22}H_{29}NO_4SNa$ (M^++Na): 426.1715, found: 426.1720.

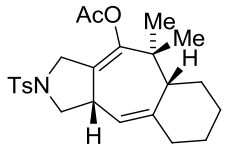
(6*R,8a*S**)-6,7-dimethyl-2-tosyl-2,3,6,8a-tetrahydro-1*H*-spiro[cyclohepta[c]pyrrole-5,1'-cyclopentan]-4-yl acetate (169k)**



Colourless solid, mp = 114-115 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.95 (d, 3H, *J* = 6.8 Hz), 1.25 (brs, 1H), 1.25-1.66 (m, 8H), 1.78-1.87 (m, 3H), 2.13 (s, 3H), 2.41 (s, 3H), 2.69 (t, 1H, *J* = 10.0 Hz), 3.36 (brs, 1H), 3.64 (d, 1H, *J* = 14.4 Hz), 3.75 (t, 1H, *J* = 8.7 Hz), 3.92 (d, 1H, *J* = 14.4 Hz), 4.99 (s, 1H), 7.31 (d, 2H, *J* = 8.0 Hz), 7.68 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 17.8, 20.5, 21.5, 24.4, 27.1, 35.3, 36.8, 40.6, 47.0, 51.0, 53.4, 55.1, 116.2, 124.6, 127.8, 129.8, 133.0, 141.3, 143.7, 146.4, 167.6; IR (NaCl, neat)

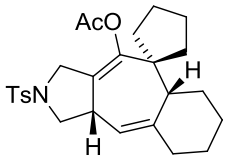
v: 2961, 2868, 1746, 1346, 1215, 1161 cm^{-1}; HRMS (ESI) calcd. for $C_{24}H_{31}NO_4SNa$ (M^++Na): 452.1871, found: 452.1869.

(3a*S,8a*R**)-9,9-dimethyl-2-tosyl-1,2,3,3a,5,6,7,8,8a,9-decahydrobenzo[4,5]cyclohepta [1,2-*c*]pyr-rol-10-yl acetate (169l)**



Colourlesss solid; mp = 160-162 °C; ^{1}H NMR ($CDCl_3$, 400MHz): δ 0.92 (s, 3H), 1.13-1.27 (m, 6H), 1.57-2.12 (m, 9H), 2.43 (s, 3H), 2.75-2.80 (m, 1H), 3.50-3.59 (m, 2H), 3.77 (t, 1H, *J* = 8.8 Hz), 3.90 (d, 1H, *J* = 14.4 Hz), 5.10 (bs, 1H), 7.33 (d, 2H, *J* = 8.0 Hz), 7.69 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100MHz): 20.4, 21.6, 24.7, 38.5, 39.9, 51.0, 55.0, 126.1, 127.9, 129.8, 132.9, 143.8, 144.7, 168.2; IR (NaCl, neat) *v*: 2936, 1749, 1346, 1216, 1161 cm^{-1}; HRMS (ESI) calcd. for $C_{24}H_{31}NO_4SNa$ (M^++Na): 452.1872, found: 454.1868.

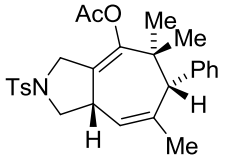
(3a*S,8a*R**)-2-tosyl-2,3,3a,5,6,7,8,8a-octahydro-1*H*-spiro[benzo[4,5]cyclohepta[1,2-*c*]pyrrole-9,1'-cyclopentan]-10-yl acetate (169m)**



Colourlesss solid; mp = 172-174 °C; ^{1}H NMR ($CDCl_3$, 400MHz): δ 1.18-1.35 (m, 4H), 1.48-1.60 (m, 4H), 1.68-1.88 (m, 8H), 2.04-2.07 (m, 1H), 2.11 (s, 3H), 2.42(s, 3H), 2.79 (t, 1H, *J* = 9.7 Hz), 3.42-3.49 (m, 1H), 3.60 (d, 1H, *J* = 14.4 Hz), 3.75 (t, 1H, *J* = 8.8 Hz),

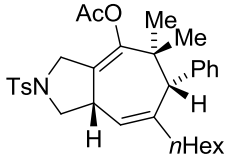
3.89 (d, 1H, *J* = 14.5 Hz), 4.99 (s, 1H), 7.32 (d, 2H, *J* = 8.2 Hz), 7.68 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100MHz): 20.5, 21.6, 24.5, 27.3, 30.3, 32.1, 35.3, 37.0, 38.9, 41.3, 51.1, 51.8, 51.9, 55.6, 114.3, 126.3, 127.9, 132.9, 143.8, 145.2, 146.4, 167.4; IR (NaCl, neat) *v*: 2936, 1749, 1346, 1215, 1161 cm^{-1}; HRMS (ESI) calcd. for $C_{26}H_{33}NO_4SNa$ (M^++Na): 478.2028, found: 478.2012.

(6*S,8a*S**)-5,5,7-trimethyl-6-phenyl-2-tosyl-1,2,3,5,6,8a-hexahydrocyclohepta[*c*]pyrrol-4-yl acetate (169n)**



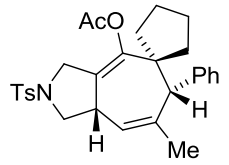
Colourless solid, mp = 166-168 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.78 (s, 3H), 1.32 (s, 3H), 1.52 (s, 3H), 1.97 (s, 3H), 2.48 (s, 3H), 2.89-2.94 (m, 2H), 3.78 (dd, 1H, *J* = 2.0, 14.4 Hz), 3.92-3.98 (m, 2H), 5.27 (s, 1H), 6.94 (d, 2H, *J* = 7.2 Hz), 7.09 (t, 2H, *J* = 7.6 Hz), 7.16-7.20 (m,1H), 7.39 (d, 2H, *J* = 7.2 Hz), 7.75 (d, 2H, *J* = 8.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 20.2, 21.6, 25.6, 26.4, 27.4, 40.2, 41.4, 51.2, 55.3, 61.3, 124.8, 126.7, 127.7, 128.0, 129.8, 132.7, 135.3, 138.0, 140.8, 143.8, 145.6, 168.8; IR (NaCl, neat) *v*: 3053, 2984, 1746, 1597, 1449, 1346, 1237 cm^{-1}; HRMS (ESI) calcd. for $C_{27}H_{31}NO_4SNa$ (M^++Na): 488.1872, found: 488.1861.

(6*S,8a*S**)-7-hexyl-5,5-dimethyl-6-phenyl-2-tosyl-1,2,3,5,6,8a-hexahydrocyclohepta[*c*]-pyrrol-4-yl acetate (169o)**



Pale-yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.80 (s, 3H), 0.84 (t, 3H, J = 7.2 Hz), 1.13-1.31 (m, 11H), 1.62-1.72 (m, 2H), 1.95 (s, 3H), 2.48 (s, 3H), 2.90-2.95 (m, 2H), 3.60-3.62 (m, 1H), 3.79 (dd, 1H, J = 2.2, 14.8 Hz), 3.89-3.97 (m, 2H), 5.24 (d, 1H, J = 2.4 Hz), 6.91 (d, 2H, J = 7.5 Hz), 7.04-7.08 (m, 2H), 7.15-7.18 (m,1H), 7.40 (d, 2H, J = 8.0 Hz), 7.76 (d, 2H, J = 8.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.0, 20.2, 21.6, 22.6, 25.7, 26.5, 28.3, 28.8, 31.6, 40.0, 40.4, 41.4, 51.2, 55.3, 59.7, 117.5, 124.6, 126.7, 127.6, 128.0, 129.8, 130.2, 132.7, 140.9, 141.9, 143.8, 145.6, 168.8; IR (NaCl, neat) v: 2953, 2928, 1748, 1597, 1348, 1209, 1163 cm^{-1}; HRMS (ESI) calcd. for $C_{32}H_{41}NO_4SNa$ (M^++Na): 558.2654, found: 558.2651.

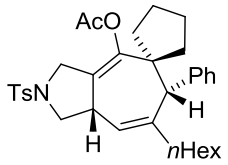
(6*S,8a*S**)-7-methyl-6-phenyl-2-tosyl-2,3,6,8a-tetrahydro-1*H*-spiro[cyclohepta[*c*]pyrro-le -5,1'-cyclopentan]-4-yl acetate (169p)**



Yellow solid; mp = 99-101 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.37-1.43 (m, 2H), 1.50 (s, 4H), 1.57 (s, 2H), 1.62-1.68 (m, 3H), 1.94 (bs, 5H), 2.47 (s, 3H), 2.96-3.02 (m, 2H), 3.52 (bs, 1H), 3.75-3.91 (m, 3H), 5.27 (s, 1H), 6.99 (d, 2H, J = 7.2 Hz), 7.11-7.19 (m, 3H),

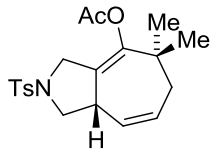
7.38 (d, 2H, *J* = 8.0 Hz), 7.75 (d, 2H, *J* = 8.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 20.3, 21.5, 23.3, 23.7, 27.3, 34.4, 46.7, 50.0, 51.4, 53.5, 55.5, 56.9, 119.0, 125.3, 126.7, 127.7, 128.0, 129.8, 133.0, 138.0, 140.9, 143.8, 146.0, 168.1; IR (NaCl, neat) *v*: 3019, 2399, 1744, 1599, 1423, 1348, 1215 cm^{-1}; HRMS (ESI) calcd. for $C_{29}H_{34}NO_4S$ (M^++H): 492.2209, found: 492.2201.

(6*S,8a*S**)-7-hexyl-6-phenyl-2-tosyl-2,3,6,8a-tetrahydro-1*H*-spiro[cyclohepta[*c*]pyrrole-5,1'-cyclopentane]-4-yl acetate (169q)**



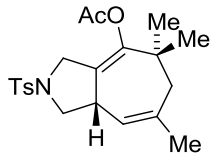
Colourlesss oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.84 (t, 3H, *J* = 7.2 Hz), 1.16-1.51 (m, 11H), 1.65-1.70 (m, 5H), 1.90-1.92 (m, 5H), 2.46 (s, 3H), 3.00 (t, 1H, *J* = 10.0 Hz), 3.06 (d, 1H, *J* = 2.6 Hz), 3.55 (t, 1H, *J* = 8.6 Hz), 3.78 (dd, 1H, *J* = 2.2, 14.8 Hz), 3.83-3.92 (m, 2H), 5.25 (s, 1H), 6.95-6.97 (m, 2H), 7.08-7.12 (m, 2H), 7.15-7.19 (m, 1H), 7.38 (d, 2H, *J* = 8.2 Hz), 7.75 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.1, 20.3, 21.6, 22.6, 23.2, 23.5, 28.4, 28.9, 31.7, 34.3, 36.6, 39.8, 40.1, 51.4, 53.6, 54.8, 55.6, 118.8, 125.2, 126.6, 127.6, 128.0, 129.8, 132.7, 141.1, 142.1, 143.8, 146.0, 167.9; IR (NaCl, neat) *v*: 2955, 2928, 1749, 1350, 1206, 1163 cm^{-1}; HRMS (ESI) calcd. for $C_{34}H_{43}NO_4SNa$ (M^++Na): 584.2810, found: 584.2815.

5,5-dimethyl-2-tosyl-1,2,3,5,6,8a-hexahydrocyclohepta[*c*]pyrrol-4-yl acetate (169r)



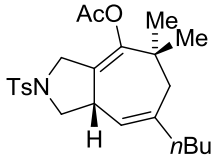
Colourless solid; mp = 146-148 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.92 (s, 3H), 1.02 (s, 3H), 1.92 (q, 1H, *J* = 7.0 Hz), 2.13 (s, 3H), 2.38 (d, 1H, *J* = 6.8 Hz), 2.43 (s, 3H), 2.85 (t, 1H, *J* = 9.2 Hz), 3.52 (d, 1H, *J* = 14.0 Hz), 3.64 (t, 1H, *J* = 9.2 Hz), 3.74 (t, 1H, *J* = 9.2 Hz), 3.86 (d, 1H, *J* = 14.0 Hz), 5.64 (d, 1H, *J* = 10.0 Hz), 5.75-5.81 (m, 1H), 7.33 (d, 2H, *J* = 8.0 Hz), 7.68 (d, 2H, *J* = 8.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 20.6, 21.6, 25.2, 28.1, 37.9, 38.2, 38.9, 50.9, 53.9, 125.6, 128.0, 129.8, 129.8, 132.3, 132.4, 143.9, 147.2, 168.0; IR (NaCl, neat) *v*: 3019, 2399, 1751, 1476, 1215, cm^{-1}; HRMS (ESI) calcd. for $C_{20}H_{25}NO_4SNa$ (M^++Na): 398.1402, found: 398.1417.

5,5,7-trimethyl-2-tosyl-1,2,3,5,6,8a-hexahydrocyclohepta[c]pyrrol-4-yl acetate (169s)



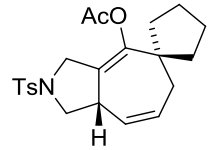
Colourlesss solid; mp = 168-170 °C; ^{1}H NMR ($CDCl_3$, 400MHz): δ 0.93 (s, 3H), 1.01 (s, 3H), 1.68-1.71 (m, 4H), 2.12 (s, 3H), 2.42 (s, 3H), 2.58 (d, 1H, *J* = 13.8 Hz), 2.80 (t, 1H, *J* = 9.6 Hz), 3.48-3.57 (m, 2H), 3.72 (t, 1H, *J* = 8.8 Hz), 3.86 (d, 1H, *J* = 14.1 Hz), 5.33 (s, 1H), 7.32 (d, 2H, *J* = 8.0 Hz), 7.68 (d, 2H, *J* = 8.1 Hz); ^{13}C NMR ($CDCl_3$, 100MHz): 20.6, 21.5, 25.4, 25.7, 28.3, 37.6, 38.2, 44.4, 50.9, 54.2, 125.8, 126.0, 128.0, 129.8, 132.3, 138.3, 143.8, 146.4, 167.9; IR (NaCl, neat) *v*: 3019, 1751, 1346, 1215, 1163 cm^{-1}; HRMS (ESI) calcd. for $C_{21}H_{27}NO_4SNa$ (M^++Na): 412.1558, found: 412.1553.

7-butyl-5,5-dimethyl-2-tosyl-1,2,3,5,6,8a-hexahydrocyclohepta[*c*]pyrrol-4-yl acetate (169t)



Colourlesss oil; ^{1}H NMR ($CDCl_3$, 400MHz): δ 0.87 (t, 3H, *J* = 7.0 Hz), 0.92 (s, 3H), 1.02 (s, 3H), 1.18-1.39 (m, 4H), 1.74 (d, 1H, *J* = 13.8 Hz), 1.96-1.98 (m, 2H), 2.15 (s, 3H), 2.43 (s, 3H), 2.54 (d, 1H, *J* = 13.8 Hz), 2.82 (t, 1H, *J* = 9.6 Hz), 3.47-3.60 (m, 2H), 3.73 (t, 1H, *J* = 8.9 Hz), 5.29 (s, 1H), 7.33 (d, 2H, *J* = 8.0 Hz), 7.68 (d, 2H, *J* = 8.1 Hz); ^{13}C NMR ($CDCl_3$, 100MHz): 14.0, 20.6, 21.5, 22.4, 25.4, 28.4, 29.6, 37.7, 38.1, 38.7, 43.3, 50.9, 54.3, 124.7, 125.9, 128.0, 129.8, 132.4, 142.4, 143.8, 146.5, 167.9; IR (NaCl, neat) *v*: 2928, 1753, 1597, 1337, 1207, 1167 cm^{-1}; HRMS (ESI) calcd. for $C_{24}H_{33}NO_4SNa$ (M^++Na): 454.2028, found: 454.2033.

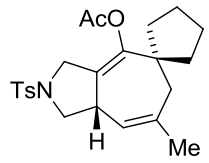
2-tosyl-2,3,6,8a-tetrahydro-1*H*-spiro[cyclohepta[*c*]pyrrole-5,1'-cyclopentan]-4-yl acetate (169u)



Yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): *δ* 1.35-1.79 (m, 11H), 2.12-2.18 (m, 3H), 2.23-2.28 (m, 1H), 2.41-2.42 (m, 3H), 2.83 (t, 1H, *J* = 9.2 Hz), 3.51 (d, 1H, *J* = 14.0 Hz), 3.66-3.69 (m, 1H), 3.75 (t, 1H, *J* = 8.8 Hz), 3.89 (d, 1H, *J* = 14.0 Hz), 5.61-5.63 (m, 1H), 5.73-5.79 (m, 1H), 7.29-7.34 (m, 2H), 7.65-7.69 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): *δ* 20.7, 21.6, 24.7, 24.9, 34.6, 35.8, 37.3, 38.4, 48.5, 51.1, 54.1, 126.1, 128.0, 129.8, 132.2, 143.9,

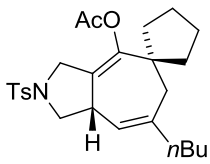
146.9, 168.2; IR (NaCl, neat) *v*: 3019, 2963, 2399, 1748, 1599, 1424, 1346, 1215 cm^{-1}; HRMS (ESI) calcd. for $C_{22}H_{27}NO_4SNa$ (M^++Na): 424.1559, found: 424.1546.

7-methyl-2-tosyl-2,3,6,8a-tetrahydro-1*H*-spiro[cyclohepta[*c*]pyrrole-5,1'-cyclopentan]-4-yl acetate (169v)



Colourlesss solid, mp = 146-148 °C; ^{1}H NMR ($CDCl_3$, 400MHz): δ 1.26-1.32 (m, 1H), 1.40-1.77 (m, 10H), 1.90 (d, 1H, *J* = 14.2 Hz), 2.11 (m, 3H), 2.37-2.41 (m, 4H), 2.78 (t, 1H, *J* = 9.6 Hz), 3.50 (d, 1H, *J* = 14.1 Hz), 3.57-3.60 (m, 1H), 3.72 (t, 1H, *J* = 8.8 Hz), 3.88 (d, 1H, *J* = 14.1 Hz), 5.32 (s, 1H), 7.31 (d, 2H, *J* = 8.1 Hz), 7.67 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100MHz): 20.7, 21.5, 24.4, 26.0, 34.5, 37.2, 38.4, 40.6, 125.7, 126.5, 128.0, 129.7, 132.3, 138.2, 143.8, 145.8, 168.1; IR (NaCl, neat) *v*: 2967, 1751, 1346, 1215, 1161 cm^{-1}; HRMS (ESI) calcd. for $C_{23}H_{29}NO_4SNa$(M^++Na): 438.1715, found: 438.1709.

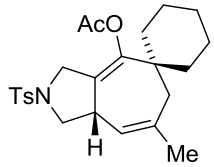
7-butyl-2-tosyl-2,3,6,8a-tetrahydro-1*H*-spiro[cyclohepta[*c*]pyrrole-5,1'-cyclopentane]-4-yl acetate (169w)



Colourlesss oil; ^{1}H NMR ($CDCl_3$, 400MHz): δ 0.87 (t, 3H, *J* = 7.1 Hz), 1.21-1.47 (m, 7H), 1.56-1.77 (m, 5H), 1.92-1.99 (m, 3H), 2.11 (s, 3H), 2.34 (d, 1H, *J* = 14.3 Hz), 2.42

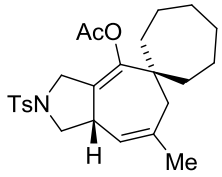
(s, 3H), 2.80 (t, 1H, *J* = 9.6 Hz), 3.51 (d, 1H, *J* = 14.0 Hz), 3.60 (t, 1H, *J* = 8.8 Hz), 3.73 (t, 1H, *J* = 8.8 Hz), 3.87 (d, 1H, *J* = 14.0 Hz), 5.28 (s, 1H), 7.31 (d, 2H, *J* = 8.1 Hz), 7.67 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100MHz): 14.0, 20.7, 21.5, 22.4, 24.4, 24.5, 29.7, 34.4, 37.2, 38.3, 39.0, 39.3, 48.5, 51.1, 54.4, 124.7, 126.4, 128.0, 129.7, 132.3, 142.4, 143.8, 145.9, 168.1; IR (NaCl, neat) *v*: 2955, 1755, 1599, 1454, 1338, 1206, 1163 cm^{-1}; HRMS (ESI) calcd. for $C_{26}H_{35}NO_4SNa$ (M^++Na): 480.2184, found: 480.2175.

7-methyl-2-tosyl-2,3,6,8a-tetrahydro-1*H*-spiro[cyclohepta[*c*]pyrrole-5,1'-cyclohexan]-4-yl acetate (169x)



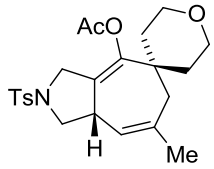
Colourlesss solid, mp = 145-146 °C; ^{1}H NMR ($CDCl_3$, 400MHz): δ 1.06-1.65 (m, 10H), 1.72 (s, 3H), 2.14-2.21 (m, 3H), 2.42-2.45 (m, 4H), 2.76-2.81 (m, 1H), 3.47-3.56 (m, 2H), 3.71 (t, 1H, *J* = 8.7 Hz), 3.87 (d, 1H, *J* = 13.8 Hz), 5.34 (s, 1H), 7.32 (d, 2H, *J* = 8.2 Hz), 7.67 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100MHz): 20.7, 21.1, 21.4, 21.5, 25.3, 25.7, 30.8, 33.9, 36.2, 38.4, 41.0, 51.1, 54.2, 126.3, 127.1, 128.0, 129.8, 132.3, 137.8, 143.8, 147.1, 168.1; IR (NaCl, neat) *v*: 2934, 1751, 1346, 1206, 1163 cm^{-1}; HRMS (ESI) calcd. for $C_{24}H_{31}NO_4SNa$ (M^++Na): 452.1872, found: 452.1878.

7-methyl-2-tosyl-2,3,6,8a-tetrahydro-1*H*-spiro[cyclohepta[*c*]pyrrole-5,1'-cycloheptan]-4-yl acetate (169y)



Pale-yellow oil; ^{1}H NMR ($CDCl_3$, 400MHz): δ 1.17-1.70 (m, 14H), 1.94-2.02 (m, 2H), 2.14 (s, 3H), 2.36-2.42 (m, 4H), 2.77-2.81 (m, 1H), 3.50-3.53 (m, 2H), 3.70 (t, 1H, *J* = 9.0 Hz), 3.85 (d, 1H, *J* = 14.4 Hz), 5.32 (s, 1H), 7.32 (d, 2H, *J* = 8.0 Hz), 7.67 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100MHz): 20.9, 21.5, 23.6, 24.2, 25.5, 31.2, 32.0, 34.9, 38.3, 42.1, 43.3, 51.0, 54.1, 124.9, 125.8, 128.0, 129.7, 138.0, 143.8, 148.5, 167.9; IR (NaCl, neat) *v*: 2926, 1751, 1346, 1215, 1161 cm^{-1}; HRMS (ESI) calcd. for $C_{25}H_{34}NO_4S$ (M^++H): 444.2209, found: 444.2200.

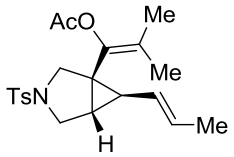
7-methyl-2-tosyl-2,2',3,3',5',6,6',8a-octahydro-1*H*-spiro[cyclohepta[*c*]pyrrole-5,4'-pyran]-4-yl acetate (169z)



Colourlesss solid, mp = 210-212 °C; ^{1}H NMR ($CDCl_3$, 400MHz): δ 1.16-1.26 (m, 2H), 1.72 (s, 4H), 1.94 (s, 1H), 2.17 (s, 3H), 2.30 (d, 1H, *J* = 14.4 Hz), 2.43 (s, 3H), 2.57 (d, 1H, *J* = 14.4 Hz), 2.76-2.81 (m, 1H), 3.46-3.67 (m, 4H), 3.73-3.75 (m, 3H), 3.90 (d, 1H, *J* = 14.2 Hz), 5.37 (s, 1H), 7.32 (d, 2H, *J* = 8.0 Hz), 7.68 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100MHz): 20.6, 21.6, 25.5, 31.0, 33.4, 38.6, 38.7, 51.1, 54.1, 63.1, 63.4, 128.0,

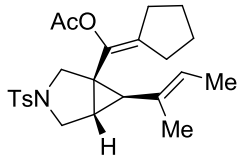
128.2, 129.8, 132.3, 136.9, 143.9, 145.5, 168.2; IR (NaCl, neat) *v*: 1751, 1346, 1204, 1163 cm^{-1}; HRMS (ESI) calcd. for $C_{23}H_{29}NO_5SNa$ (M^++Na): 454.1664, found: 454.1664.

2-methyl-1-((1*S,5*S**,6*S**)-6-((*E*)-prop-1-en-1-yl)-3-tosyl-3-azabicyclo[3.1.0]hexan-1-yl)-prop-1-en-1-yl acetate (173a)**



Colourlesss oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.38 (t, 1H, *J* = 3.8 Hz), 1.51 (s, 3H), 1.57 (s, 3H), 1.60 (d, 3H, *J* = 6.5 Hz), 1.72 (dd, 1H, *J* = 4.0, 9.2 Hz), 1.99 (s, 3H), 2.41 (s, 3H), 3.09 (dd, 1H, *J* = 3.6, 9.4 Hz), 3.26 (d, 1H, *J* = 9.3 Hz), 3.56 (d, 1H, *J* = 9.4 Hz), 3.70 (d, 1H, *J* = 9.4 Hz), 4.92-4.98 (m, 1H), 5.40-5.48 (m, 1H), 7.30 (d, 2H, *J* = 8.0 Hz), 7.65 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 17.9, 17.9, 18.6, 20.4, 21.5, 30.5, 34.5, 49.7, 53.6, 125.4, 125.8, 127.5, 128.0, 129.6, 133.6, 138.0, 143.4, 169.2; IR (NaCl, neat) *v*: 2918, 2857, 2255, 1746, 1346, 1217, 1165 cm^{-1}; HRMS (ESI) calcd. for $C_{21}H_{28}NO_4S$ (M^++H): 390.1739, found: 390.1733.

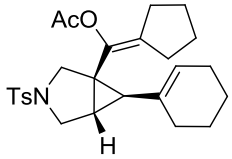
((1*S,5*S**,6*R**)-6-((*E*)-but-2-en-2-yl)-3-tosyl-3-azabicyclo[3.1.0]hexan-1-yl)(cyclopentylidene)methyl acetate (173k)**



Colourlesss oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.48-1.66 (m, 11H), 1.75 (t, 1H, *J* = 4.2 Hz), 1.98 (s, 3H), 2.03-2.13 (m, 4H), 2.42 (s, 3H), 3.15 (dd, 1H, *J* = 3.9, 9.3 Hz), 3.29 (d,

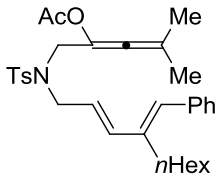
1H, *J* = 9.4 Hz), 3.55 (d, 1H, *J* = 9.3 Hz), 3.76 (d, 1H, *J* = 9.4 Hz), 5.12 (q, 1H, *J* = 6.2 Hz), 7.31 (d, 2H, *J* = 8.0 Hz), 7.67 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 13.6, 15.2, 20.4, 21.5, 25.7, 26.6, 26.8, 29.2, 29.4, 34.5, 35.2, 49.9, 53.9, 120.3, 127.5, 129.6, 130.7, 133.8, 135.7, 135.9, 143.3, 169.0; IR (NaCl, neat) *v*: 2963, 2872, 1748, 1346, 1215, 1163 cm^{-1}; HRMS (ESI) calcd. for $C_{24}H_{31}NO_4SNa$ (M^++Na): 452.1871, found: 452.1876.

((1*S,5*S**,6*R**)-6-(cyclohex-1-en-1-yl)-3-tosyl-3-azabicyclo[3.1.0]hexan-1-yl)(cyclopentylidene) methyl acetate (173m)**



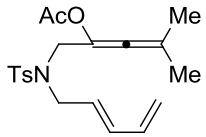
Colourlesss oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.44-1.60 (m, 8H), 1.62-1.68 (m, 1H), 1.70-1.75 (m, 3H), 1.94 (bs, 2H), 1.99 (s, 3H), 2.08-2.11 (m, 4H), 2.42 (s, 3H), 3.14 (dd, 1H, *J* = 3.8, 9.2 Hz), 3.30 (d, 1H, *J* = 9.4 Hz), 3.54 (d, 1H, *J* = 9.3 Hz), 3.75 (d, 1H, *J* = 9.4 Hz), 5.26 (s, 1H), 7.31 (d, 2H, *J* = 8.0 Hz), 7.65 (d, 2H, *J* = 8.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 20.5, 21.5, 22.4, 23.0, 25.4, 25.8, 26.1, 26.9, 28.1, 29.2, 29.5, 33.2, 35.4, 49.9, 53.8, 122.7, 127.5, 129.6, 132.6, 133.7, 135.6, 136.0, 143.3, 169.1; IR (NaCl, neat) *v*: 3021, 2932, 1742, 1346, 1223, 1163 cm^{-1}; HRMS (ESI) calcd. for $C_{26}H_{33}NO_4SNa$ (M^++Na): 478.2028, found: 478.2022.

1-(*N*-((2*E*,4*E*)-4-benzylidenedec-2-en-1-yl)-4-methylphenylsulfonamido)-4-methylpenta-2,3-dien-2-yl acetate (174o)



Colourlesss oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.89 (t, 3H, J = 6.8 Hz), 1.26-1.42 (m, 8H), 1.80 (s, 6H), 2.06 (s, 3H), 2.24-2.28 (m, 2H), 2.41 (s, 3H), 3.98 (s, 2H), 4.04 (d, 2H, J = 6.8 Hz), 5.33 (dt, 1H, J = 6.8, 15.6 Hz), 6.12 (d, 1H, J = 15.6 Hz), 6.35 (s, 1H), 7.22-7.35 (m, 7H), 7.72 (d, 2H, J = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.1, 20.9, 21.4, 21.5, 22.7, 27.5, 28.7, 29.0, 29.6, 31.6, 47.5, 48.7, 109.2, 114.3, 122.0, 126.8, 127.2, 128.3, 128.7, 129.6, 131.5, 137.4, 138.2, 138.8, 139.8, 143.0, 168.9, 193.3; IR (NaCl, neat) v: 2926, 1983, 1753, 1597, 1445, 1348, 1213, 1161 cm^{-1}; HRMS (ESI) calcd. for $C_{32}H_{41}NO_4SNa$ (M^++Na): 558.2654, found: 558.2658.

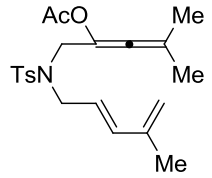
(*E*)-4-methyl-1-(4-methyl-N-(penta-2,4-dienyl)phenylsulfonamido)penta-2,3-dien-2-yl acetate (174r)



Colourlesss oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.77 (s, 6H), 2.03 (s, 3H), 2.41 (s, 3H), 3.92 (s, 4H), 5.05-5.15 (m, 2H), 5.44-5.40 (m, 1H), 6.07 (t, 1H, J = 12.4 Hz), 6.17 (m, 1H), 7.27 (d, 2H, J = 8.0 Hz), 7.70 (d, 2H, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 20.9, 21.3, 21.5, 28.6, 47.6, 48.2, 109.3, 114.3, 117.9, 127.2, 127.5, 127.8, 129.5, 129.6, 135.0, 135.9, 137.9, 143.1, 168.9, 193.2; IR (NaCl, neat) v: 3019, 2913, 2399, 1983, 1748,

1346, 1215 cm^{-1}; HRMS (ESI) calcd. for $C_{20}H_{25}NO_4SNa$ (M^++Na): 398.1402, found: 398.1398.

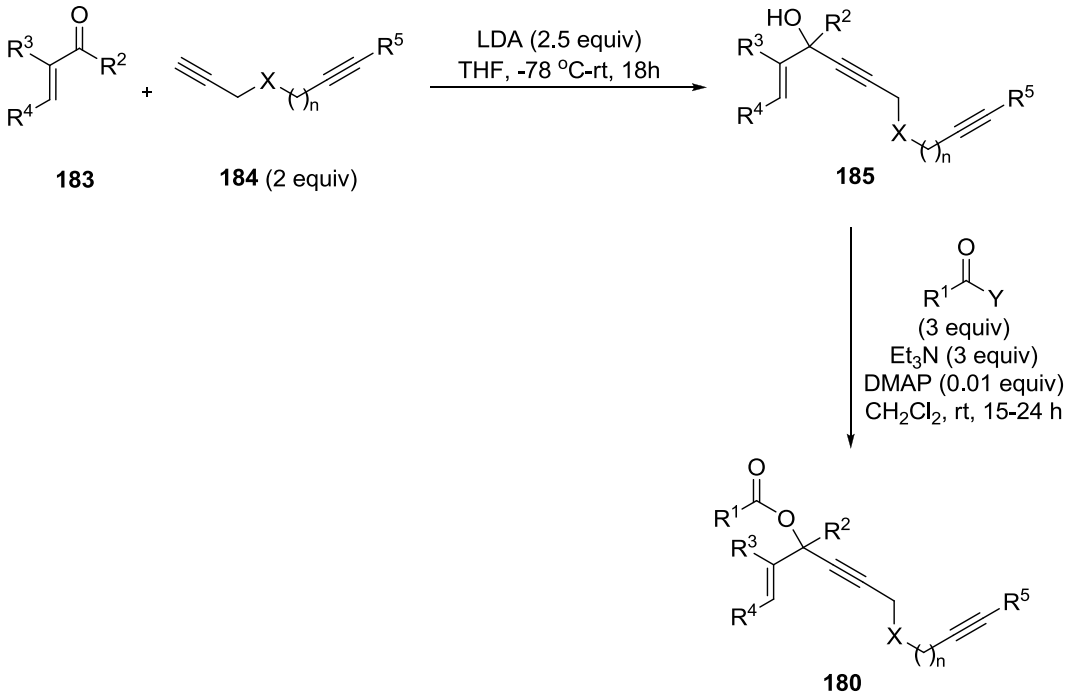
(*E*)-4-methyl-1-(4-methyl-*N*-(4-methylpenta-2,4-dien-1-yl)phenylsulfonamido)penta-2,3-dien-2-yl acetate (174s)



Colourlesss oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.69 (s, 3H), 1.77 (s, 6H), 2.02 (s, 3H), 2.40 (s, 3H), 3.93-3.96 (m, 4H), 4.88 (s, 1H), 4.94 (s, 1H), 5.33 (dt, 1H, J = 6.8, 15.6 Hz), 6.14 (d, 1H, J = 15.6 Hz), 7.26 (d, 2H, J = 8.0 Hz), 7.69 (d, 2H, J = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 18.4, 20.9, 21.3, 21.4, 28.6, 47.6, 48.4, 109.3, 114.3, 117.0, 123.3, 127.2, 129.5, 137.2, 138.0, 141.1, 143.1, 168.8, 193.2; IR (NaCl, neat) v: 3021, 2916, 1983, 1748, 1346, 1215 cm^{-1}; HRMS (ESI) calcd. for $C_{21}H_{27}NO_4SNa$ (M^++Na): 412.1558, found: 412.1561.

7.4 Gold Catalyzed Cycloisomerizations of 1-Ene-4,*m*-Diyne Esters: A Route to Prepare Spirocyclic Compounds

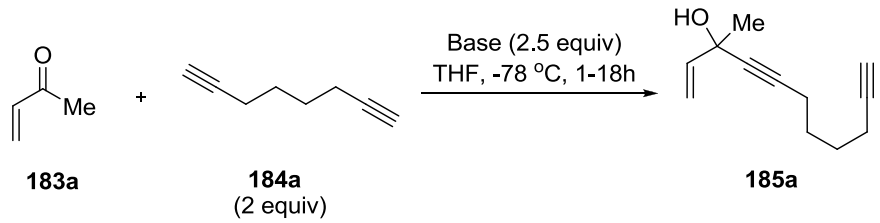
General Experimental Procedure for the Synthesis of 1-Ene-4,*m*-Diyne Esters 180a-d and 180g-m



To a stirred solution of the appropriate 1,*n*-diyne **184** (10.0 mmol) in THF (40 mL) was added LDA (6.3 mL, 12.5 mmol, 2.0 M in THF) at −78 °C and left to stir for 1 hour. A solution of the respective α,β−unsaturated ketone **183** (5 mmol) in THF (10 mL) was subsequently added dropwise to the solution at −78 °C and the reaction mixture was stirred overnight. The reaction mixture was then quenched with saturated NH_4Cl (25 mL) and extracted with EtOAc (3 x 25 mL). The combined organic layers were washed with brine (25 mL), dried over $MgSO_4$, concentrated under reduced pressure and purified by flash column chromatography on silica gel with *n*Hex:EtOAc = 9:1 to 4:1 as eluent to

furnish alcohols **185** which, with or without characterisation, were directly employed in the next reaction. To a solution of resulting alcohol (1 mmol) in anhydrous CH_2Cl_2 (10 mL), R^1COCl or anhydride (3.00 mmol), DMAP (0.10 mmol,) and Et_3N (3.00 mmol) were added in and left to stir for 0.5 h at 0 °C. The solution was then brought to room temperature and left to stir overnight. The mixture was quenched with saturated $NaHCO_3$ (10 mL) and extracted with CH_2Cl_2 (3 x 10 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure and purified by flash column chromatography *n*Hex:EtOAc = 9:1 to 5:1 to give 1-ene-4,*m*-diyne esters **180** in 20-38% yields over two steps.

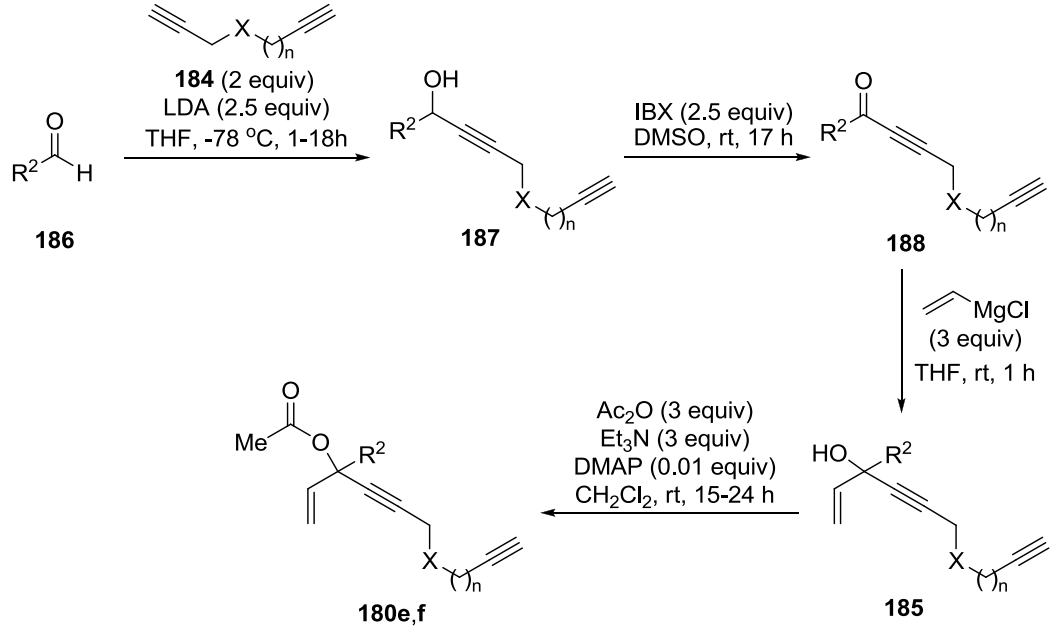
General Experimental Procedure for the Optimizing the Synthesis of Alcohol 185



183a **184a** (2 equiv) **185a**

To a stirred solution of the 1,8-octadiyne **184a** (4.0 mmol) in THF (10 mL) was added appropriate base (5 mmol) at −78 °C and left to stir for 1 hour. A solution of the methyl vinyl ketone **183a** (2 mmol) in THF (2 mL) was subsequently added dropwise to the solution at −78 °C and the reaction mixture was stirred overnight. Upon completion indicated via TLC analysis, the reaction mixture was then quenched with saturated NH_4Cl (10 mL) and extracted with EtOAc (3 x 10 mL). The combined organic layers were washed with brine (10 mL), dried over $MgSO_4$, concentrated under reduced pressure and purified by flash column chromatography on silica gel with *n*Hex:EtOAc = 9:1 to 4:1 as eluent to furnish alcohol **185a** in low yields of 8-38%.

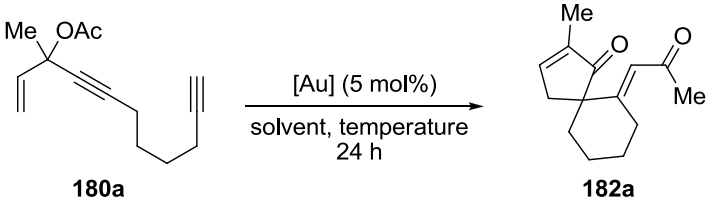
General Procedure for the Synthesis of 1-Ene-4,*m*-Diyne Esters 180e and 180f from Aldehydes 186



To a stirred solution of the appropriate 1,*n*-diyne **184** (10.0 mmol) in THF (40 mL) was added LDA (6.3 mL, 12.5 mmol, 2.0 M in THF) at −78 °C and left to stir for 1 hour. A solution of the respective aldehyde **186** (5 mmol) in THF (10 mL) was subsequently added dropwise to the solution at −78 °C and the reaction mixture was stirred overnight. The reaction mixture was then quenched with saturated NH_4Cl (25 mL) and extracted with EtOAc (3 x 25 mL). The combined organic layers were washed with brine (25 mL), dried over $MgSO_4$, concentrated under reduced pressure and purified by flash column chromatography on silica gel with *n*Hex:EtOAc = 9:1 to 4:1 as eluent to furnish alcohols **187** in 55-80% yield which, without characterisation, were directly employed in the next reaction. To a solution of resulting alcohol (3 mmol) in in DMSO (20 mL) was added IBX (2.5 equiv) portionwise and the resulting mixture was left to stir overnight. The reaction mixture was then quenched with water (10 mL) and EtOAc (10 mL) were added

into the reaction flask and stirred for another 15 minutes. The mixture was then filtered through Celite© and the aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic layers were washed again with water (2 x 10 mL), brine (10 mL), dried over MgSO4 and concentrated under reduced pressure. The crude mixture was used directly without further purification. To a stirred solution containing crude mixture of ketone **188** was added vinylmagnesium chloride (5.6 mL, 9 mmol, 1.6 M in THF) and stirred for 1 hour. Upon completion, the reaction mixture was quenched with saturated NH_4Cl (10 mL) and extracted with EtOAc (2 x 10 mL). The combined organic layers were washed with brine (10 mL), dried over MgSO4, concentrated under reduced pressure and purified by flash column chromatography on silica gel with *n*Hex:EtOAc = 9:1 to 4:1 as eluent to furnish alcohol **185a** in 50-60% yield which, without characterization, was directly employed to the next step. To a solution of resulting alcohol (1 mmol) in anhydrous CH_2Cl_2 (10 mL), acetic anhydride (3.00 mmol), DMAP (0.10 mmol,) and Et_3N (3.00 mmol) were added in and left to stir for 0.5 h at 0 °C. The solution was then brought to room temperature and left to stir overnight. The mixture was quenched with saturated $NaHCO_3$ (10 mL) and extracted with CH_2Cl_2 (3 x 10 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure and purified by flash column chromatography with *n*Hex:EtOAc = 9:1 to 5:1 as eluent to give 1-ene-4,*m*-diyne esters **180** in 75-95% yields.

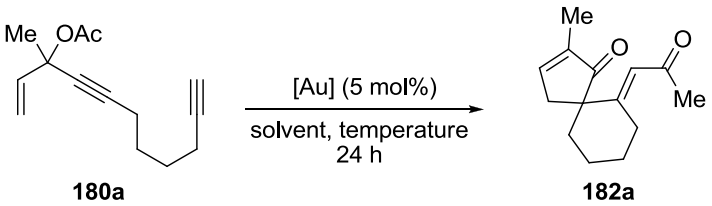
General Experimental Procedure for Optimizing Gold(I) Catalyzed Cycloisomerization of 1-Ene-4,10-Diyne Esters 180a



180a **182a**

To a solution of 1-ene-4,10-diyne ester **180a** (0.2 mmol) with or without drying agent (80 mg) in dry solvent was added gold(I) or gold(III) catalysts (10 μmol) under argon atmosphere. The mixture was left to stir at specified temperature and the reaction was monitored via TLC method. Upon completion, the reaction mixture was left to cool to room temperature, filtered through Celite©, washed with EtOAc and solvent was removed under reduced pressure. Purification via flash column chromatography on silica gel with *n*Hex:EtOAc = 9:1 as eluent furnished the corresponding spiro adduct **182a**.

General Experimental Procedure for Optimizing Enantioselective Gold(I) Catalyzed Cycloisomerization of 1-Ene-4,10-Diyne Ester 180a

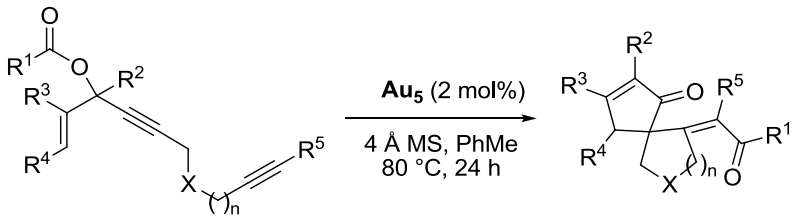


180a **182a**

Gold(I) catalyst $AuSMe_2Cl$ (10 µmol) and chiral ligand (5.0 µmol) were stirred in anhydrous CH_2Cl_2 (1.0 mL) for 1 h before the solvent was removed in vacuo. $AgSbF_6$ (10.0 µmol),4Å molecular sieves (80.0 mg) and toluene (1.0 mL) were then added into the reaction flask and the mixture was stirred for 0.5 h. A solution of 1-ene-4,10-diyne ester **180a** in toluene (1.0 mL) was added in slowly and the reaction mixture was left to

stir. Upon completion indicated by TLC analysis, the mixture was filtered through Celite© and purified via flash colum chromatography with *n*Hex:EtOAc = 9:1 as eluent to yield the expected adducts **182a**. Ee value was determined using Chiralpak OC-H HPLC column with *n*Hex/ ^{i}PrOH = 9:1 as eluent.

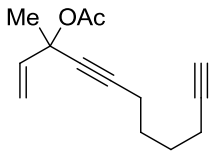
General Experimental Procedure for Gold(I) Catalyzed Cycloisomerization of 1-Ene-4,*m*-Diyne Esters 180



180 **182**

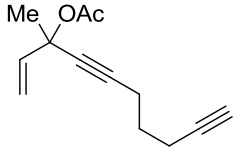
To a solution of the appropriate 1-ene-4,10-diyne ester **180** (0.2 mmol) and 4 Å molecular sieves (80 mg) in anhydrous toluene (2 mL) was added $\mathbf{Au_5}$ (10 μmol) under argon atmosphere. The mixture was heated to 80 °C and left to stir for 24h. Upon completion, the reaction mixture was left to cool to room temperature before filtered through Celite©, washed with EtOAc and solvent was removed under reduced pressure. Purification via flash column chromatography on silica gel with *n*Hex:EtOAc = 9:1 to 4:1 as eluent furnished the corresponding spiro adduct **182**.

3-methylundeca-1-en-4,10-diyn-3-yl acetate (180a)



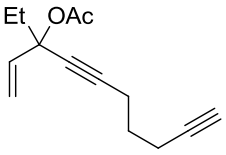
Yield 82%; yellow oil; ^{1}H NMR ($CDCl_{3,}$ 300 MHz): δ 1.64-1.55 (7H, m), 1.91 (1H, t, J = 2.7 Hz), 1.97 (3H, s), 2.28-2.13 (4H, m), 5.14 (1H, d, J = 10.5 Hz), 5.47 (1H, d, J = 17.1), 5.95 (1H, dd, J = 10.5, 17.1 Hz); ^{13}C NMR ($CDCl_{3,}$ 75 MHz): δ 17.9, 18.2, 21.9, 27.4, 27.4, 28.6, 68.5, 74.8, 79.1, 84.0, 86.7, 114.9, 139.3, 168.9; IR (NaCl, neat) v: 3298, 2931, 1740, 1368, 1237 cm^{-1}; HRMS (ESI) calcd. for $C_{14}H_{18}O_2Na$ (M^++Na): 241.1204, found: 241.1205.

3-methyldeca-1-en-4,9-diyn-3-yl acetate (180b)



Yield 43%; yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.66 (3H, s), 1.74 (2H, q, J = 6.8 Hz), 1.94 (1H, t, J = 2.6 Hz), 2.01 (3H, s), 2.30 (2H, td, J = 2.6, 6.8 Hz), 2.38 (2H, t, J = 7.2 Hz), 5.18 (1H, dd, J = 0.4, 10.4 Hz), 5.52 (1H, dd, J = 0.4, 17.2 Hz), 5.97 (1H, dd, J = 10.4, 17.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 17.5, 17.9, 21.9, 27.4, 28.6, 68.8, 74.8, 79.5, 83.5, 86.1, 115.0, 139.3, 169.0; IR (NaCl, neat) v: 3298, 2934, 1746, 1352, 1240 cm^{-1}. HRMS (ESI) calcd. for $C_{13}H_{16}O_2Na$ (M^++Na): 227.1048, found: 227.1048.

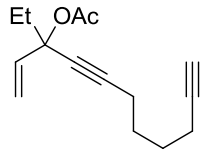
3-ethyldeca-1-en-4,9-diyn-3-yl acetate (180c)



Yield 75%; yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz,): δ 0.97 (3H, t, J = 7.6 Hz), 1.71-1.85 (3H, m), 1.93-2.01 (2H, m), 2.02 (3H, s), 2.32 (2H, td, J = 2.8, 7.2 Hz), 2.41 (2H, t, J =

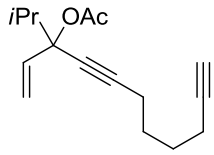
7.2 Hz), 5.24 (1H, dd, *J* = 0.4, 10.4 Hz), 5.51 (1H, dd, *J* = 17.0 Hz), 5.86 (1H, dd, *J* = 10.4; 17.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 8.4, 17.5, 17.9, 21.9, 27.5, 34.1, 68.8, 78.2, 78.9, 83.5, 87.1, 116.2, 138.1, 168.9; IR (NaCl, neat) *v*: 3296, 2974, 2245, 1744, 1368, 1234 cm^{-1}; HRMS (ESI) calcd. for $C_{14}H_{18}O_2Na$ (M^++Na): 241.1204, found: 241.1205.

3-ethylundeca-1-en-4,10-diyn-3-yl acetate (180d)



Yield 80%; yellow oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 0.90 (3H, t, *J* = 7.4 Hz), 1.63-1.53 (4H, m), 1.78-1.67 (1H, m), 1.99-1.84 (5H, m), 2.18-2.10 (2H, m), 2.27-2.20 (2H, m), 5.16 (1H, d, *J* = 10.5, 1.1 Hz), 5.44 (1H, d, *J* = 17.1, 1.1 Hz), 5.79 (1H, dd, *J* = 17.1, 10.5 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz,): δ 8.3, 17.8, 18.2, 21.7, 27.4, 34.0, 68.5, 77.7, 78.8, 83.9, 87.7, 116.1, 138.1, 168.7; IR (NaCl, neat) *v*: 3298, 2934, 1744, 1643, 1366, 1236 cm^{-1}; HRMS (ESI) calcd. for $C_{15}H_{20}O_2Na$ (M^++Na): 255.1361, found: 255.1361.

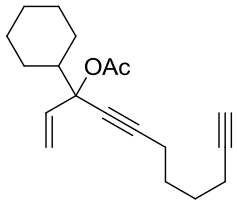
3-isopropylundeca-1-en-4,10-diyn-3-yl acetate (180e)



Yield 50%; yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz,): δ 0.90-0.92 (2H, d, *J* = 6.8 Hz), 1.02-1.04 (3H, d, *J* = 6.8 Hz), 1.63-1.66 (4H, m), 1.97-1.98 (4H, m),), 2.04-2.14 (1H, m), 2.20-2.24 (2H, m), 2.29 (2H, m), 5.24-5.27 (1H, dd, *J* = 0.9, 10.4 Hz 5.46-5.51 (1H, dd, *J*

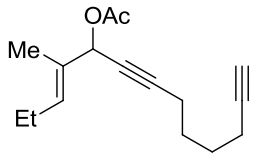
= 0.9, 17.2 Hz), 5.77-5.84 (1H, dd, *J* = 17.2, 10.3 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 16.9, 17.0, 17.8, 18.1, 21.5, 27.5,27.6, 37.2, 68.2, 76.6, 82.0, 84.1, 88.1, 116.6, 137.3, 168.5; IR (NaCl, neat) *v*: 1237, 1643, 1743, 2934, 3298 cm^{-1}; HRMS (ESI) calcd. for $C_{16}H_{22}O_2Na$ (M^++Na): 269.1517, found: 269.1519.

3-cyclohexylundeca-1-en-4,10-diyn-3-yl acetate (180f)



Yield 56%; yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.11-1.28 (5H, m), 1.63-1.66 (5H, m), 1.72-1.75 (4H, m), 1.92-1.94 (1H, m), 2.00 (3H, s), 2.18-2.23 (2H, m), 2.28-2.32 (2H, m), 5.26 (1H, dd, *J* = 10.4, 1.1 Hz), 5.49 (1H, dd, *J* = 16.8, 1.2 Hz), 5.81 (1H, dd, *J* = 17.2, 1.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 17.9, 18.3, 21.9, 26.1, 26.2, 26.2, 26.4, 27.1, 27.3, 27.5, 46.7, 68.5, 81.9, 84.0, 88.3, 117.0, 137.2, 168.9; IR (NaCl, neat) *v*: 3298, 2934, 1743, 1643, 1237 cm^{-1}; HRMS (ESI) calcd. for $C_{19}H_{26}O_2Na$ (M^++Na): 309.1830, found: 309.1833.

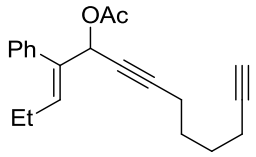
(E)-4-methyltrideca-3-en-6,12-diyn-5-yl acetate (180g)



Yield 94%; yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.96 (3H, t, *J* = 7.6 Hz), 1.58-1.68 (4H, m), 1.68 (3H, s), 1.91-1.93 (1H, m), 2.00-2.07 (5H, m), 2.17-2.20 (4H, m), 5.63 (1H, t, *J* = 6.8 Hz), 5.73 (1H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 13.6, 15.1, 17.9, 18.3, 19.0,

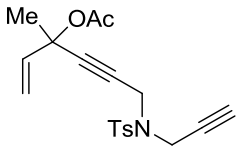
21.1, 27.5, 27.7, 68.5, 76.8, 84.0, 86.6, 94.5, 130.4, 132.3, 146.5, 169.9; IR (NaCl, neat) *v*: 3296, 2931, 1744, 1643, 1238 cm^{-1}; HRMS (ESI) calcd. for $C_{16}H_{23}O_2Na$ (M^++Na): 247.1698, found: 247.1693.

(E)-4-phenyltrideca-3-en-6,12-diyn-5-yl acetate (180h)



Yield 75%; yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz,): δ 0.94 (3H, t, J = 7.6 Hz), 1.59-1.53 (4H, m), 1.94-1.89 (2H, m), 1.96 (3H, s), 1.98 (1H, t, J = 5.2 Hz), 2.18-2.14 (2H, m), 2.24-2.20 (2H, m), 6.01 (1H, t, J = 7.6 Hz), 6.05 (1H, t, J = 7.2 Hz), 7.36-7.19 (5H, m); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 13.7, 17.8, 18.2, 20.8, 22.1, 27.4, 27.5, 68.1, 68.3, 76.6, 84.0, 87.8, 127.2, 128.0, 129.3, 134.6, 136.5, 137.4, 169.4; IR (NaCl, neat) *v*: 3298, 2934, 1744, 1643, 1366, 1236 cm^{-1}; HRMS (ESI) calcd. for $C_{21}H_{24}O_2Na$ (M^++Na): 331.1674, found: 331.1677.

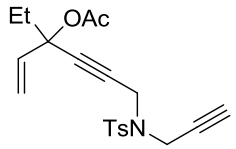
3-methyl-6-(4-methyl-N-(prop-2-ynyl)phenylsulfonamido)hex-1-en-4-yn-3-yl acetate (180i)



Yield 85%; yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.51 (3H, s), 1.99 (3H, s), 2.15 (1H, t, J = 2.4 Hz), 2.41 (3H, s), 4.17 (2H, d, J = 2.4 Hz), 4.25 (2H, s), 5.14 (1H, d, J = 10.4 Hz), 5.35 (1H, d, J = 17.2 Hz), 5.83 (1H, dd, J = 10.4, 17.2 Hz), 7.29 (2H, d, J = 8.4

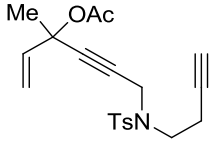
Hz), 7.71 (2H, d, *J* = 8.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.5, 21.7, 28.0, 36.2, 36.6, 73.8, 73.9, 76.4, 79.2, 84.5, 115.5, 127.8, 129.6, 135.3, 138.3, 143.8, 168.7; IR (NaCl, neat) *v*: 3296, 2938, 2862, 1746, 1368, 1236 cm^{-1}; HRMS (ESI) calcd. for $C_{19}H_{21}NO_4SNa$ (M^++Na): 382.1089, found: 382.1089.

3-ethyl-6-(4-methyl-N-(prop-2-ynyl)phenylsulfonamido)hex-1-en-4-yn-3-yl acetate (180j)



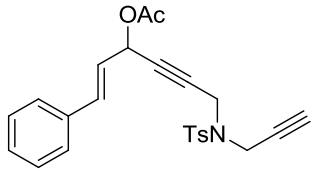
Yield 83%; yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.80 (3H, t, *J* = 7.6 Hz), 1.63 (1H, dqn, *J* = 7.6, 13.6 Hz), 1.79 (1H, dqn, *J* = 7.6, 13.6 Hz), 1.94 (3H, s), 2.11 (1H, t, *J* = 2.4 Hz), 2.37 (3H, s), 4.14 (2H, d, *J* = 2.4 Hz), 4.22 (2H, s), 5.14 (1H, dd, *J* = 0.4, 10.4 Hz), 5.29 (1H, dd, *J* 0.4, 17.2 Hz), 5.66 (1H, dd, *J* = 10.4, 17.2 Hz), 7.25 (2H, d, *J* = 8.4 Hz), 7.67 (2H, d, *J* = 8.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 8.1, 21.5, 21.6, 33.7, 36.2, 36.6, 73.9, 76.3, 77.9, 80.1, 83.4, 116.6, 127.8, 129.6, 135.3, 137.1, 143.8, 168.6; IR (NaCl, neat) *v*: 3304, 2978, 1746, 1352, 1236 cm^{-1}; HRMS (ESI) calcd. for $C_{20}H_{23}NO_4SNa$ (M^++Na): 396.1245, found: 396.1245.

6-(N-(but-3-ynyl)-4-methylphenylsulfonamido)-3-methylhex-1-en-4-yn-3-yl acetate (180k)



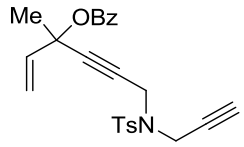
Yield 94%; yellow oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.42 (3H, s), 1.95 (3H, s), 1.98 (1H, t, J = 2.6 Hz), 2.38 (3H, s), 2.50 (2H, td, J = 2.6, 7.2 Hz), 3.35 (2H, t, J = 7.2 Hz), 4.26 (2H, s), 5.07 (1H, d, J = 10.4 Hz), 5.21 (1H, d, J = 17.0 Hz), 5.76 (1H, dd, J = 10.4, 17.0 Hz), 7.26 (2H, d, J = 8.3 Hz), 7.70 (2H, d, J = 8.3 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 18.9, 21.5, 21.6, 27.9, 37.6, 45.3, 70.2, 73.7, 79.5, 80.8, 84.4, 115.3, 127.6, 129.7, 136.0, 138.2, 143.5, 168.6; IR (NaCl, neat) v: 3292, 2934, 1742, 1597, 1368, 1238 cm^{-1}; HRMS (ESI) calcd. for $C_{20}H_{23}NO_4SNa$ (M^++Na): 396.1245, found: 396.1245.

6-(N-(but-3-ynyl)-4-methylphenylsulfonamido)-3-methylhex-1-en-4-yn-3-yl acetate (180l)



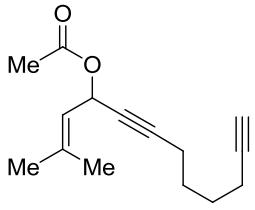
Yield 90%; yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.09 (3H, s), 2.16-2.18 (1H, m), 2.34 (3H, s), 4.15-4.16 (2H, m), 4.28 (2H, s), 5.86-5.88 (1H, m), 6.04-6.09 (1H, dd, J = 6.4, 15.6 Hz), 6.67-6.71 (1H, m), 7.25-7.38 (7H, m), 7.72-7.74 (2H, m); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.0, 21.5, 36.5, 36.6, 64.0, 74.2, 76.3, 79.8, 81.6, 123.2, 126.9, 127.9, 128.6, 128.7, 129.6, 134.7, 135.2, 135.5, 144.01, 169.6; IR (NaCl, neat) v: 3293, 2930, 1743, 1598, 1368, 1240 cm^{-1}; HRMS (ESI) calcd. for $C_{24}H_{23}NO_4SNa$ (M^++Na): 444.1245, found: 444.1248.

3-methyl-6-(4-methyl-N-(prop-2-ynyl)phenylsulfonamido)hex-1-en-4-yn-3-yl benzoate (180m)



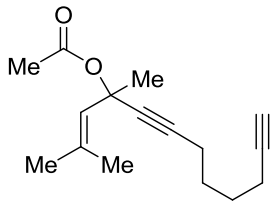
Yield 38%; yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.66 (3H, s), 2.11-2.13 (1H, t, *J* = 2.4 Hz), 2.30 (3H, s), 4.20 (2H, d, *J* = 2.8), 4.29 (2H, s), 5.19-5.22 (1H, dd, *J* = 0.9, 10.4 Hz), 5.44-5.48 (1H, dd, *J* = 0.9, 17.2 Hz), 5.91-5.98 (1H, dd, *J* = 10.3, 17.2 Hz), 7.19-7.21 (2H, m), 7.41-7.50 (4H, m), 7.68-7.71 (1H, m), 7.96-7.99 (2H, m); ^{13}C NMR ($CDCl_3$, 100 MHz): *δ* 18.9, 21.5, 27.9, 73.9, 74.3, 76.5, 79.5, 84.5, 115.8, 127.8, 128.4, 128.5, 129.6, 130.2, 130.6, 133.0, 133.8, 135.3, 138.3, 143.8, 164.0; IR (NaCl, neat) *v*: 3292, 2934, 1742, 1597, 1368, 1238 cm^{-1}; HRMS (ESI) calcd. for $C_{24}H_{24}NO_4S$ (M^++H): 422.1426, found: 422.1425.

2-methyldodeca-2-en-5,11-diyn-4-yl acetate (180n)



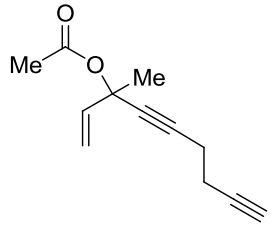
Yield 43%; yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): *δ* 1.46 (7H, s), 1.59-1.63 (6H, m), 1.93 (3H, s), 1.96-1.98 (1H, m), 2.18-2.20 (2H, m), 2.22-2.33 (2H, m), 5.58 (1H, dt, *J* = 2.0, 16.4 Hz), 6.18-6.22 (1H, d, *J* = 16.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): *δ* 17.6, 19.2, 21.8, 25.0, 68.5, 79.9, 80.1, 84.9, 96.1, 117.0, 139.6, 169.8; IR (NaCl, neat) *v*: 3301, 2929, 1745, 1648, 1357, 1236, 1164 cm^{-1}; HRMS (ESI) calcd. for $C_{15}H_{20}O_2Na$ (M^++Na): 255.1361, found: 255.1360.

2,4-dimethyldodeca-2-en-5,11-diyn-4-yl acetate (180o)



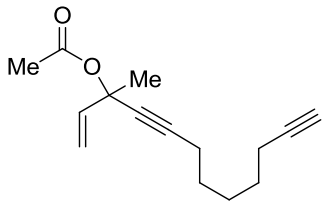
Yield 43%; yellow oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.58 (6H, s), 1.60-1.67 (4H, m), 1.83 (3H, s), 1.92 (1H, t, J = 2.7 Hz), 1.96 (3H, s), 2.12-2.25 (2H, m), 2.31-2.38 (2H, m), 5.80 (1H, s); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 17.9, 19.1, 21.8, 25.0, 27.0, 27.5, 68.5, 79.7, 80.1, 83.9, 96.1, 117.0, 139.6, 169.8; IR (NaCl, neat) v: 3300, 2926, 1742, 1645, 1352, 1236, 1163 cm^{-1}; HRMS (ESI) calcd. for $C_{16}H_{22}O_2Na$ (M^++Na): 269.1517, found: 269.1518.

3-methylnona-1-en-4,8-diyn-3-yl acetate (180p)



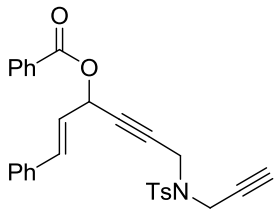
Yield 50%; yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.65 (3H, s), 1.98 (1H, t, J = 2.4 Hz), 1.99 (3H, s), 2.36-2.42 (2H, m), 2.44-2.49 (2H, m), 5.17 (1H, dd, J = 0.4, 10.4 Hz), 5.53 (1H, dd, J = 0.4, 17.0 Hz), 5.96 (1H, dd, J = 10.4, 17.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 18.6, 18.9, 21.9, 28.6, 69.3, 74.7, 79.8, 82.5, 85.3, 115.2, 139.1, 168.9; IR (NaCl, neat) v: 3307, 2939, 1742, 1368, 1240 cm^{-1}; HRMS (ESI) calcd. for $C_{12}H_{14}O_2Na$ (M^++Na): 213.0891, found: 213.0891.

3-methyldodeca-1-en-4,11-diyn-3-yl acetate (180q)



Yield 78%; yellow oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.48-1.60 (6H, m), 1.67 (3H, s), 1.92 (1H, t, J = 2.7 Hz), 2.01 (3H, s), 2.14-2.30 (4H, m), 5.18 (1H, d, J = 10.4 Hz), 5.51 (1H, d, J = 17.1 Hz), 5.99 (1H, dd, J = 10.4, 17.1 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 18.2, 18.6, 21.9, 27.8, 27.9, 28.0, 28.6, 68.3, 74.8, 78.9, 84.3, 87.1, 114.9, 139.4, 168.9;IR (NaCl, neat) v: 3296, 2986, 2936, 1746, 1368, 1236 cm^{-1}; HRMS (ESI) calcd. for $C_{15}H_{20}O_2Na$ (M^++Na): 255.1361, found: 255.1361.

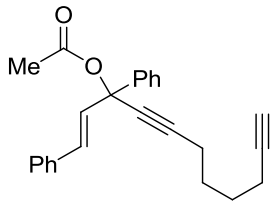
(E)-6-(4-methyl-N-(prop-2-ynyl)phenylsulfonamido)-1-phenylhex-1-en-4-yn-3-yl benzoate (180r)



Yield 67%; yellow solid; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.18-2.19 (1H, m), 2.28 (3H, s), 4.19 (2H, d, J = 2.4Hz), 4.34 (2H, d, J = 1.6 Hz), 6.13-6.15 (1H, m), 6.22-6.24 (1H, m), 6.80 (1H, d, J = 15.2 Hz), 7.22 (1H, d, J = 8.0 Hz), 7.31-7.41 (6H, m), 7.45-7.50 (4H, m), 7.57-7.62 (2H, m), 7.74 (2H, d, J = 8.4 Hz), 8.06-8.08 (2H, m), 8.13-8.15 (2H, m); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.4, 36.6, 36.7, 64.6, 74.2, 76.4, 80.0, 81.7, 123.3, 127.0, 127.9, 128.0, 128.5, 128.6, 128.7, 129.6, 129.8, 130.2, 133.4, 133.8, 135.2, 135.5, 144.1,

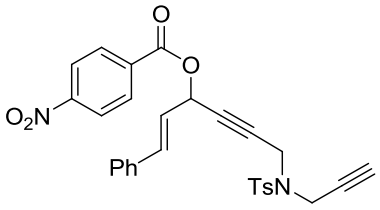
165.3; IR (NaCl, neat) *v*: 3298, 2985, 2940, 1748, 1365, 1238 cm^{-1}; HRMS (ESI) calcd. for $C_{29}H_{25}NO_4SNa$ (M^++Na): 506.1402, found: 506.1402.

(E)-1,3-diphenylundeca-1-en-4,10-diyn-3-yl acetate (180s)



Yield 69%; white solid; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.87-1.73 (4H, m), 1.99-2.03 (1H, m), 2.16 (3H, s), 2.30 (2H, t, *J* = 6.5 Hz), 2.59 (2H, t, *J* = 6.5 Hz), 6.52 (1H, d, *J* = 8.5 Hz), 7.01 (1H, d, *J* = 8.5 Hz), 7.28-7.42 (6H, m), 7.50 (2H, d, *J* = 7.5 Hz), 7.66 (2H, d, *J* = 8.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 18.0, 19.3, 21.3, 27.6, 68.7, 74.9, 77.3, 84.1, 98.5, 126.4, 126.4, 126.6, 128.1, 128.4, 128.7, 132.8, 137.4, 139.9, 169.8; IR (NaCl, neat) *v*: 3296, 2986, 2936, 1746, 1368, 1236 cm^{-1}; HRMS (ESI) calcd. for $C_{25}H_{24}O_2Na$ (M^++Na): 379.1674, found: 379.1674.

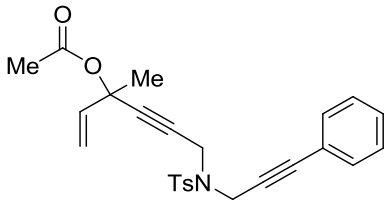
(E)-6-(4-methyl-N-(prop-2-ynyl)phenylsulfonamido)-1-phenylhex-1-en-4-yn-3-yl 4-nitrobenzoate (180t)



Yield 68%; yellow solid; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.14-2.16 (1H, m), 2.32 (3H, s), 4.11-4.31 (4H, m), 6.14-6.24 (2H, m), 6.83 (2H, d, *J* = 15.6 Hz), 7.24-7.42 (7H, m), 7.69-7.74 (2H, m), 8.22-8.23 (2H, m), 8.23-8.24 (2H, m); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.5,

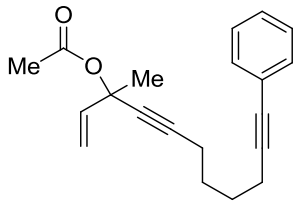
36.4, 36.5, 36.6, 37.0, 65.7, 74.3, 76.2, 80.8, 80.9, 112.3, 122.5, 123.6, 123.6, 127.0, 127.2, 127.9, 127.9,128.8, 128.9, 129.0, 129.5, 129.6, 130.8, 131.0, 135.1, 135.2, 135.7, 140.4, 144.1, 150.8, 163.4; IR (NaCl, neat) *v*: 3296, 2986, 2936, 1746, 1368, 1236 cm^{-1}; HRMS (ESI) calcd. for $C_{29}H_{24}N_2O_6SNa$ (M^++Na): 551.1253, found: 551.1255.

3-methyl-6-(4-methyl-N-(3-phenylprop-2-ynyl)phenylsulfonamido)hex-1-en-4-yn-3-yl acetate (180χ)



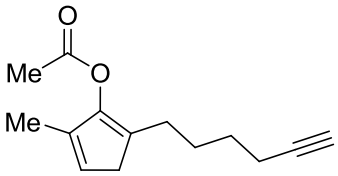
Yield 39%; yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.54 (3H, s), 1.97 (3H, s), 2.34 (3H, s), 4.28 (2H, s), 4.41 (2H, s), 5.13-5.16 (1H, dd, *J* = 0.9, 10.3 Hz), 5.38-5.42 (1H, dd, *J* = 0.9, 17.0 Hz), 5.82-5.89 (1H, dd, *J* = 10.3, 17.1 Hz), 7.15-7.18 (2H, d, *J* = 8.0 Hz), 7.22-7.28 (5H, m), 7.73-7.75 (2H, d, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.5, 21.7, 28.1, 29.7, 37.2, 73.9, 79.5, 81.5, 84.5, 85.7, 115.6, 122.2, 127.9, 128.2, 128.5, 129.7, 131.6, 135.3, 138.4, 143.8, 168.7; IR (NaCl, neat) *v*: 3292, 2987, 2936, 1746, 1368, 1236 cm^{-1}; HRMS (ESI) calcd. for $C_{25}H_{26}NO_4SNa$ (M^++Na): 436.1583, found: 436.1584.

3-methyl-11-phenylundeca-1-en-4,10-diyn-3-yl acetate (180δ)



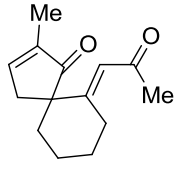
Yield 33%; yellow oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.68-1.73 (7H, m), 2.02 (3H, s), 2.33 (2H, t, J = 6.3 Hz), 2.44 (2H, t, J = 6.3 Hz), 5.18 (1H, dd, J = 0.9, 10.2 Hz), 5.53 (1H, dd, J = 0.9, 17.1 Hz), 6.02 (1H, dd, J = 10.3, 17.0 Hz), 7.25-7.29 (3H, m), 7.38-7.41 (2H, m); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 18.4, 18.9, 21.9, 27.8, 28.7, 74.9, 79.1, 80.9, 86.9, 89.8, 124.0, 127.5, 128.2, 131.5, 139.4, 168.9; IR (NaCl, neat) v: 3298, 2989, 2937, 1748, 1368, 1236 cm^{-1}; HRMS (ESI) calcd. for $C_{20}H_{23}O_2Na$ (M^++Na): 295.1698, found: 295.1702.

2-(hex-5-ynyl)-5-methylcyclopenta-1,4-dienyl acetate (181a)



Yield 52%; yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.47-1.62 (4H, m), 1.80 (3H, d, J = 2.0 Hz), 1.93 (1H, t, J = 2.7 Hz), 2.19 (2H, td, J = 2.7, 6.8 Hz), 2.22-2.29 (5H, m), 2.82-2.86 (2H, m), 5.89-5.93 (1H, m); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 12.4, 18.2, 20.5, 25.9, 28.1, 28.2, 38.2, 68.3, 84.4, 124.4, 130.1, 138.1, 147.2, 169.2.

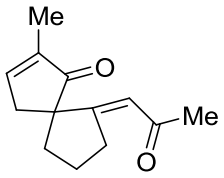
(E)-2-methyl-6-(2-oxopropylidene)spiro[4.4]non-2-en-1-one (182a)



Yield 89%; yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.38-1.64 (3H, m), 1.76-1.98 (7H, m), 2.12 (3H, s), 2.55 (1H, dqn, J = 2.0, 18.8 Hz), 2.71 (1H, dqn, J = 2.4, 18.8 Hz), 3.84-3.77 (1H, m), 5.73 (1H, d, J = 1.2 Hz), 7.21-7.24 (1H, m); ^{13}C NMR ($CDCl_3$, 100 MHz):

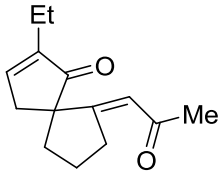
δ 10.3, 22.9, 26.5, 27.5, 32.3, 36.3, 41.6, 55.1, 121.3, 140.6, 155.3, 159.2, 199.7, 210.8; IR (NaCl, neat) *v*: 2934, 1694, 1641, 1609, 1447, 1194 cm^{-1}; HRMS (ESI) calcd. for $C_{14}H_{18}O_2Na$ (M^++Na): 241.1204, found: 241.1209.

(E)-2-methyl-6-(2-oxopropylidene)spiro[4.4]non-2-en-1-one (182b)



Yield 67%; yellow oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.62-1.69 (1H, m), 1.71-1.79 (1H, m), 1.81 (3H, d, *J* = 1.0 Hz), 1.99-2.11 (2H, m), 2.12 (3H, s), 2.54-2.67 (2H, m), 2.86 (1H, m), 2.96-3.06 (1H, m), 5.77 (1H, t, *J* = 2.5 Hz), 7.35-7.39 (1H, m); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 10.6, 24.4, 31.4, 34.1, 37.5, 44.5, 60.0, 119.0, 140.8, 156.4, 170.2, 198.1, 210.2; IR (NaCl, neat) *v*: 2953, 2922, 1694, 1636, 1608, 1435, 1193 cm^{-1}; HRMS (ESI) calcd. for $C_{13}H_{16}O_2Na$ (M^++Na): 227.1048, found: 227.1048.

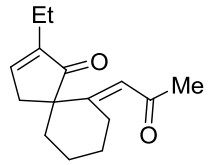
(E)-2-ethyl-6-(2-oxopropylidene)spiro[4.4]non-2-en-1-one (182c)



Yield 68%; yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.12 (3H, t, *J* = 7.6 Hz), 1.61-1.70 (1H, m), 1.71-1.83 (1H, m), 1.99-2.11 (2H, m), 2.12 (3H, s), 2.22 (2H, m), 2.54-2.69 (2H, m), 2.87 (1H, m), 2.95-3.07 (1H, m), 5.77 (1H, t, *J* = 2.6 Hz), 7.32-7.34 (1H, m); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 11.9, 18.4, 24.4, 31.4, 34.1, 37.4, 44.5, 60.4, 118.9, 146.8,

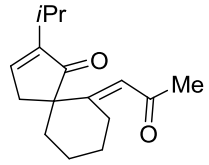
154.7, 170.2, 198.0, 209.7; IR (NaCl, neat) *v*: 2965, 1694, 1634, 1611, 1460, 1366, 1194 cm^{-1}; HRMS (ESI) calcd. for $C_{14}H_{18}O_2Na$ (M^++Na): 241.1204, found: 241.1205.

(E)-2-ethyl-6-(2-oxopropylidene)spiro[4.5]dec-2-en-1-one (182d)



Yield 65%; yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.11 (3H, t, *J* = 7.6 Hz), 1.37-1.64 (3H, m), 1.76-1.98 (4H, m), 2.12 (3H, s), 2.23 (2H, qd, *J* = 1.8, 7.6 Hz), 2.57 (1H, dqn, *J* = 2.0, 18.8 Hz), 2.72 (1H, dqn, *J* = 2.4, 18.8 Hz), 3.85-3.76 (1H, m), 5.74 (1H, d, *J* = 1.2 Hz), 7.21-7.17 (1H, m); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 11.9, 18.2, 22.9, 26.5, 27.5, 32.2, 36.2, 41.5, 55.5, 121.2, 146.6, 153.5, 159.3, 199.7, 210.4; IR (NaCl, neat) *v*: 2934, 1694, 1636, 1609, 1449, 1354, 1223 cm^{-1}; HRMS (ESI) calcd. for $C_{15}H_{20}O_2Na$ (M^++Na): 255.1361, found: 255.1361.

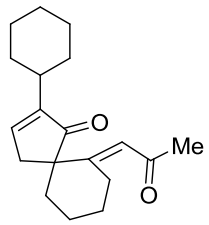
(E)-2-isopropyl-6-(2-oxopropylidene)spiro[4.5]dec-2-en-1-one (182e)



Yield 62%; yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.10-1.12 (6H, m), 1.43-1.58 (3H, m), 1.79-1.84 (3H, m), 1.87-1.97 (1H, m), 2.12 (3H, s), 2.53-2.72 (3H, m), 3.78-3.82 (1H, d, *J* = 14.4 Hz), 5.73 (1H, s), 7.15 (1H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.0, 21.3, 22.8, 24.8, 26.5, 27.4, 32.2, 36.1, 41.3, 55.6, 121.2, 151.1, 152.1, 159.5, 199.7, 210.0; IR

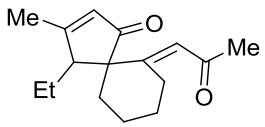
(NaCl, neat) *v*: 2934, 1694, 1636, 1609, 1449, 1354, 1223 cm^{-1}; HRMS (ESI) calcd. for $C_{16}H_{22}O_2Na$ (M^++Na): 269.1517, found: 269.1515.

(E)-2-cyclohexyl-6-(2-oxopropylidene)spiro[4.5]dec-2-en-1-one (182f)



Yield 42%; yellow oil; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.12-1.23 (3H, m), 1.32-1.54 (5H, m), 1.69-1.92 (9H, m), 2.11 (3H, s), 2.30-2.37 (1H, m), 2.52-2.57 (1H, m), 2.72-2.66 (1H, m), 3.77-3.81 (1H, m), 5.72-5.73 (1H, d, *J* = 1.6 Hz), 7.12-7.13 (1H, m); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 22.8, 26.2, 26.3, 26.3, 26.5, 27.4, 31.6, 32.0,32.2, 34.2, 36.1, 41.5, 55.5, 121.2, 150.1, 152.6, 159.5, 200.0, 210.1; IR (NaCl, neat) *v*: 2937, 1698, 1635, 1446, 1354, 1221 cm^{-1}; HRMS (ESI) calcd. for $C_{19}H_{26}O_2Na$ (M^++Na): 309.1830, found: 309.1830.

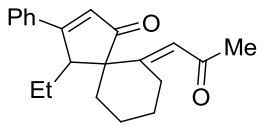
(E)-4-ethyl-3-methyl-6-(2-oxopropylidene)spiro[4.5]dec-2-en-1-one (182g)



Yield 32%; yellow oil; ^1H NMR ($CDCl_3$, 400 MHz): δ 0.81-0.84 (3H, t, *J* = 7.2 Hz), 1.38-1.51 (2H, m), 1.55-1.67 (1H, m), 1.71-1.95 (7H, m), 2.07 (3H, s), 2.11 (3H, s), 2.14 (1H, m), 2.80-2.81 (1H, m), 3.64-3.68 (1H, m), 5.66 (1H, s), 5.94 (1H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 11.6, 18.6, 21.0, 22.7, 26.8, 27.4, 29.6, 32.2, 54.7, 59.8, 121.9,

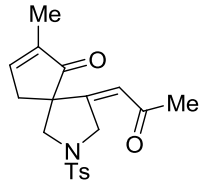
129.0, 162.1, 178.4, 199.7, 210.2; IR (NaCl, neat) *v*: 2934, 1694, 1636, 1609, 1449, 1354, 1223 cm^{-1}; HRMS (ESI) calcd. for $C_{16}H_{22}O_2Na$ (M^++Na): 269.1517, found: 269.1515.

(E)-4-ethyl-6-(2-oxopropylidene)-3-phenylspiro[4.5]dec-2-en-1-one (182h)



Yield 30%; yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.60-0.64 (3H, t, *J* = 7.2 Hz), 1.45-1.50 (1H, m), 1.62-1.71 (1H, m), 1.83-1.91 (5H, m), 2.03-2.11 (4H, m), 2.16-2.23 (1H, m), 3.53-3.56 (1H, t, *J* = 4.4 Hz), 3.78-3.82 (1H, m), 5.70 (1H, s), 6.52 (1H, s), 7.44-7.47 (3H, m), 7.58-7.61 (2H, m); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 11.2, 22.3, 23.0, 27.0, 27.3, 29.1, 32.2, 50.5, 60.3, 122.4, 126.4, 126.9, 129.0, 131.1, 134.0, 162.0, 175.0, 199.5, 210.1; IR (NaCl, neat) *v*: 2935, 1698, 1612, 1448, 1351, 1226 cm^{-1}; HRMS (ESI) calcd. for $C_{21}H_{24}O_2Na$ (M^++Na): 331.1674, found: 331.1675.

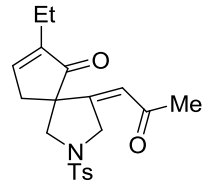
(Z)-7-methyl-4-(2-oxopropylidene)-2-tosyl-2-azaspiro[4.4]non-7-en-6-one (182i)



Yield 44%; yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.84 (3H, d, *J* = 1.6 Hz), 2.12 (3H, s), 2.43 (3H, s), 2.70 (1H, dqn, *J* = 2.4, 19.2 Hz), 2.91 (1H, dqn, *J* = 2.4, 19.2 Hz), 3.10 (1H, d, *J* = 9.2 Hz), 3.46 (1H, d, *J* = 9.2 Hz), 3.92 (1H, dd, *J* = *2.8*, 18.8 Hz), 4.71 (1H, dd, *J* = 2.4, 18.8 Hz), 5.73 (1H, t, *J* = 2.8 Hz), 7.33 (2H, d, *J* = 8.2 Hz), 7.43-7.47 (1H, m), 7.71 (2H, d, *J* = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 10.5, 21.6, 31.2, 44.4, 53.7,

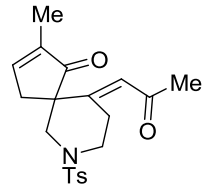
56.5, 58.2, 118.7, 128.1, 129.9, 131.9, 141.6, 144.2, 157.4, 160.4, 197.0, 205.9; IR (NaCl, neat) *v*: 2965, 1699, 1626, 1350, 1166 cm^{-1}; HRMS (ESI) calcd. for $C_{19}H_{21}NO_4SNa$ (M^++Na): 382.1089, found: 382.1089.

(Z)-7-ethyl-4-(2-oxopropylidene)-2-tosyl-2-azaspiro[4.4]non-7-en-6-one (182j)



Yield 34%; yellow oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.13 (3H, t, *J* = 7.5 Hz), 2.12 (3H, s), 2.19-2.26 (2H, m), 2.43 (3H, s), 2.71 (1H, dqn, *J* = 2.0, 19.3 Hz), 2.91 (1H, dqn, *J* = 2.5, 19.3 Hz), 3.11 (1H, d, *J* = 9.0 Hz), 3.46 (1H, d, *J* = 9.0 Hz), 3.92 (1H, dd, *J* = 2.5, 19.0 Hz), 4.71 (1H, dd, *J* = 2.0, 19.0 Hz), 5.72 (1H, t, *J* = 2.5 Hz), 7.33 (2H, d, *J* = 8.3 Hz), 7.40-7.43 (1H, m), 7.71 (2H, d, *J* = 8.3 Hz) ; ^{13}C NMR ($CDCl_3$, 125 MHz): δ 11.9, 18.4, 21.6, 31.3, 44.4, 53.7, 56.5, 58.6, 118.6, 128.1, 129.9, 131.4, 144.2, 147.6, 155.8, 160.5, 197.0, 205.5; IR (NaCl, neat) *v*: 2968, 1701, 1624, 1350, 1165 cm^{-1}; HRMS (ESI) calcd. for $C_{20}H_{23}NO_4SNa$ (M^++Na): 396.1245, found: 396.1245.

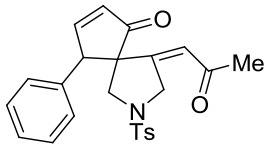
(E)-2-methyl-10-(2-oxopropylidene)-7-tosyl-7-azaspiro[4.5]dec-2-en-1-one (182k)



Yield 72%; yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.82 (3H, d, *J* = 1.2 Hz), 2.09 (3H, s), 2.27-2.33 (2H, m), 2.40 (3H, s), 2.47 (1H, d, *J* = 11.2 Hz), 2.54 (1H, m), 3.13 (1H, m),

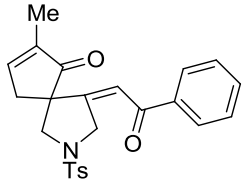
3.40 (1H, dd, *J* = 2.4, 11.2 Hz), 3.80-4.00 (2H, m), 5.75 (1H, s), 7.28 (2H, d, *J* = 8.0 Hz), 7.35-7.39 (1H, m), 7.55 (2H, d, *J* = 8.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 10.2, 21.5, 26.5, 32.1, 41.2, 46.4, 53.8, 54.4, 122.7, 129.9, 132.7, 140.7, 144.0, 153.0, 157.2, 199.1, 207.6; IR (NaCl, neat) *v*: 2970, 1700, 1620, 1350, 1166 cm^{-1}; HRMS (ESI) calcd. for $C_{20}H_{23}NO_4SNa$ (M^++Na): 396.1245, found: 396.1245.

(Z)-4-(2-oxopropylidene)-9-phenyl-2-tosyl-2-azaspiro[4.4]non-7-en-6-one (182l)



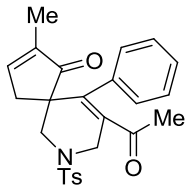
Yield 30%; yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.11-2.18 (3H, m), 2.41 (3H, s), 2.47 (1H, s), 2.82 (1H, d, *J* = 10.0 Hz), 2.97 (1H, d, *J* = 10.0 Hz), 3.95 (1H, d, *J* = 2.4 Hz), 4.16-4.17 (1H, m), 4.67 (1H, d, *J* = 2.4 Hz), 5.98-5.99 (1H, m), 6.52-6.54 (1H, m), 7.02-7.04 (2H, m), 7.38-7.41 (3H, m), 7.58 (2H, d, *J* = 8.4 Hz), 7.85-7.88 (1H, m); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.5, 31.3, 51.5, 53.1, 60.0, 62.5, 118.5, 127.7, 128.0, 128.4, 128.7, 128.7, 129.2, 129.7, 129.8, 132.0, 133.5, 135.6, 143.8, 160.7, 165.4, 196.9, 205.5; IR (NaCl, neat) *v*: 2974, 1701, 1624, 1352, 1168 cm^{-1}; HRMS (ESI) calcd. for $C_{24}H_{23}NO_4SNa$ (M^++Na): 444.1245, found: 444.1245.

(Z)-7-methyl-4-(2-oxo-2-phenylethylidene)-2-tosyl-2-azaspiro[4.4]non-7-en-6-one (182m)



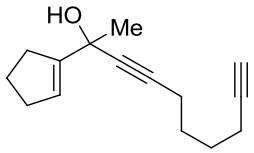
Yield 38%; yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.74-1.75 (3H, m), 2.27-2.33 (1H, m), 2.40-2.46 (4H, m), 2.52-2.53 (1H, m), 3.12-3.17 (1H, m), 3.41-3.46 (1H, m), 3.48-3.50 (1H, d, J = 10.8 Hz), 3.63-3.66 (1H, d, J = 10.8 Hz), 6.42 (1H, s), 7.22 (1H, m), 7.26-7.29 (2H, m), 7.43-7.49 (3H, m), 7.57-7.61 (3H, m), 7.83-7.85 (2H, m), 8.09-8.11 (1H, m); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 10.5, 21.6, 34.7, 40.9, 57.9, 59.6, 121.1, 127.8, 128.5, 128.5, 128.8, 129.8, 130.2, 130.7, 133.5, 133.7, 136.1, 141.5, 144.1, 156.8, 196.2, 208.3; IR (NaCl, neat) v: 2970, 1700, 1620, 1350, 1166 cm^{-1}; HRMS (ESI) calcd. for $C_{24}H_{23}NO_4SNa$ (M^++Na): 444.1245, found: 444.1246.

9-acetyl-2-methyl-10-phenyl-7-tosyl-7-azaspiro[4.5]deca-2,9-dien-1-one (182χ)



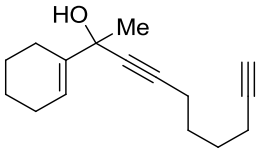
Yield 49%; yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.45 (3H, s), 1.62-1.63 (3H, s), 2.44 (3H, s), 2.74-2.80 (2H, m), 2.92-2.97 (1H, d, J = 19.6 Hz), 3.20-3.24 (1H, d, J = 16.4 Hz), 3.52-3.54 (1H, d, J = 10.4 Hz), 4.55-4.59 (1H, m), 6.99-7.01 (2H, m), 7.19 (1H, m), 7.23-7.35 (5H, m), 7.65-7.67 (2H, d, J = 8.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 10.2, 21.6, 30.7, 40.2, 46.0, 52.4, 54.6, 127.8, 128.5, 128.9, 129.4, 130.0, 132.4, 136.6, 136.7, 141.7, 144.1, 145.5, 158.1, 200.6, 207.9; IR (NaCl, neat) v: 2973, 1701, 1625, 1351, 1166; HRMS (ESI) calcd. for $C_{25}H_{26}NO_4SNa$ (M^++Na): 436.1583, found: 436.1584.

2-cyclopentenyldeca-3,9-diyn-2-ol (185u)



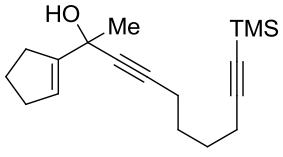
Yield 61%; yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.57 (3H, s), 1.63 (4H, qn, J = 3.2 Hz), 1.88-1.97 (3H, m), 2.00 (1H, s), 2.19-2.27 (4H, m), 2.32-2.39 (2H, m), 2.40-2.47 (2H, m), 5.76-5.79 (1H, m); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 18.0, 18.2, 23.7, 27.5, 27.6, 29.3, 31.2, 32.3, 67.4, 68.5, 83.3, 83.7, 84.1, 125.1, 148.1.

2-cyclohexenyldeca-3,9-diyn-2-ol (185v)



Yield 70%; yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.52 (3H, s), 1.53-1.72 (8H, m), 1.89 (1H, s), 1.94 (1H, t, J = 2.4 Hz), 2.03-2.10 (2H, m), 2.11-2.17 (2H, m), 2.18-2.28 (4H, m), 6.00 (1H, tt, J = 1.5, 3.8 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 18.0, 18.2, 22.3, 22.9, 24.0, 25.0, 27.6, 27.6, 29.2, 68.5, 70.6, 84.0, 84.0, 84.1, 121.2, 140.7.

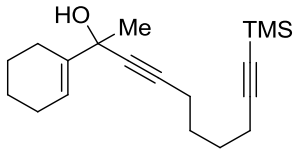
2-cyclopentenyl-10-(trimethylsilyl)deca-3,9-diyn-2-ol (185w)



Yield 62%; yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.12 (9H, s), 1.63 (4H, m), 1.91-1.96 (2H, m), 1.98 (1H, s), 2.23-2.26 (4H, m), 2.33-2.46 (4H, m), 5.77-5.78 (1H, m); ^{13}C

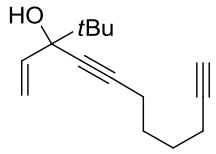
NMR ($CDCl_3$, 100 MHz): δ 0.2, 18.2, 19.4, 23.7, 27.7, 27.7, 29.3, 31.2, 32.3, 67.4, 83.5, 83.6, 84.7, 107.0, 125.1, 148.1.

2-cyclohexenyl-10-(trimethylsilyl)deca-3,9-diyn-2-ol (185x)



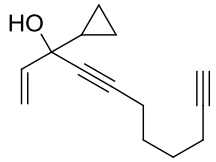
Yield 68%; yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.14 (9H, s), 1.53 (3H, s), 1.59-1.63 (7H, m), 1.87 (1H, s), 2.05- 2.07 (2H, m), 2.13-2.14 (2H, m), 2.22-2.27 (5H, m), 6.00-6.02 (1H, m); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 18.3, 19.4, 21.5, 22.3, 22.9,24.0, 25.0, 27.7, 29.2, 70.6, 83.9, 84.1, 84.7, 107.0, 121.2, 140.7.

3-tert-butylundeca-1-en-4,10-diyn-3-ol (185y)



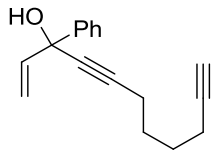
Yield 47%; yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.62-1.66 (4H, m), 1.90 (1H, s), 1.94 (1H, t, J = 2.4 Hz), 2.19-2.23 (2H, m), 2.26-2.29 (2H, m), 5.16 (1H, d, J = 10.4 Hz), 5.47 (1H, d J = 16.8 Hz), 5.98 (1H, dd, J = 10.4, 17.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 17.9, 18.2, 25.1, 27.5, 27.6, 38.4, 68.6, 77.3, 81.3, 84.1, 86.2, 115.2, 139.1.

3-cyclopropylundeca-1-en-4,10-diyn-3-ol (185z)



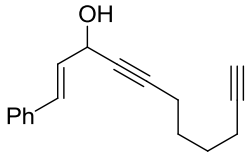
Yield 34%; yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.41-0.48 (3H, m), 0.59-0.62 (1H, m) 1.11-1.15 (1H, m), 1.56-1.61 (4H, m), 1.92-1.94 (1H, m), 2.17-2.24 (5H, m), 5.09 (1H, d, J = 10.4 Hz), 5.46 (1H, d, J = 17.2 Hz), 5.96 (1H, dd, J = 10.4, 17.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 17.9, 18.1, 20.9, 27.5, 27.5, 68.6, 73.1, 78.9, 84.0, 86.1, 113.6, 141.0.

3-phenylundeca-1-en-4,10-diyn-3-ol (185α)



Yield 44%; yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.95-1.96 (4H, m), 2.20-2.21 (1H, m), 2.22-2.24 (2H, m), 2.33-2.36 (2H, m), 2.56 (1H, s), 5.14-5.16 (1H, dd, J = 3.2, 10.1 Hz), 5.54-5.58 (1H, dd, J = 2.4, 16.9 Hz), 6.01-6.08 (1H, dd, J = 2.4, 16.9 Hz), 7.24-7.29 (1H, m), 7.32-7.36 (2H, m), 7.60-7.62 (2H, m); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 18.0, 18.4, 27.5, 27.6, 68.7, 73.2, 81.5, 84.1, 87.7, 113.5, 125.8, 127.8, 128.3, 142.0, 143.6.

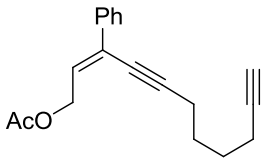
(E)-1-phenylundeca-1-en-4,10-diyn-3-ol (185β)



Yield 76%; yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.63-1.71 (4H, m), 1.95-1.96 (2H, m), 2.22-2.26 (2H, m), 2.30-2.33 (2H, m), 5.04 (1H, s), 6.30 (1H, dd, J = 5.6, 15.6 Hz), 6.76 (1H, d, J = 15.6 Hz), 7.24-7.26 (1H, m), 7.31-7.35 (2H, m), 7.40-7.42 (2H, m); ^{13}C

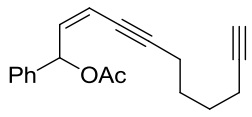
NMR ($CDCl_3$, 100 MHz): δ 18.0, 18.4, 27.5, 27.5, 63.1, 68.8, 80.0, 84.2, 86.7, 126.8, 128.0, 128.6, 128.8, 131.5, 136.3

(Z)-3-phenylundeca-2-en-4,10-diynyl acetate (189α)



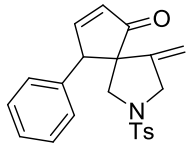
Yield 40%; yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.58-1.68 (4H, m), 1.88-1.89 (1H, m), 2.00 (3H, s), 2.14-2.18 (2H, m), 2.41 (2H, t, J = 6.4 Hz), 4.90 (2H, d, J = 6.8 Hz), 6.29-6.32 (1H, t, J = 6.8 Hz), 7.16-7.27 (3H, m), 7.50-7.53 (2H, m); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 18.0, 19.2, 21.0, 27.6, 27.6, 63.6, 68.7, 76.8, 84.0, 98.3, 126.3, 127.4, 128.3, 128.4, 128.9, 137.4, 170.9; IR (NaCl, neat) v: 2970, 1705, 1623, 1355, 1169; HRMS (ESI) calcd. for $C_{19}H_{20}NO_2SNa$ (M^++Na): 303.1361, found: 303.1363.

(Z)-1-phenylundeca-2-en-4,10-diynyl acetate (189β)



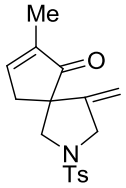
Yield 83%; yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.59-1.67 (8H, m), 1.96-1.99 (2H, m), 2.06-2.07 (6H, m), 2.19-2.24 (4H, m), 2.30-2.33 (4H, m), 5.69-5.73 (1H, m), 6.11-6.16 (1H, m), 6.20-6.26 (1H, m), 6.82-6.86 (1H, d, J = 16.0 Hz), 7.25-7.38 (7H, m), 7.41-7.43 (2H, m); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 17.8, 18.3, 20.9, 27.4, 27.6, 64.5, 68.3, 75.3, 78.1, 84.1, 87.6, 112.7, 124.6, 126.8, 128.3, 133.7, 135.9, 139.2, 169.6; IR (NaCl, neat) v: 2971, 1706, 1623, 1358, 1170; HRMS (ESI) calcd. for $C_{19}H_{20}NO_2SNa$ (M^++Na): 303.1361, found: 303.1361.

4-methylene-9-phenyl-2-tosyl-2-azaspiro[4.4]non-7-en-6-one (190l)



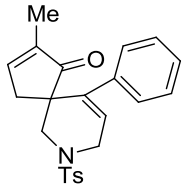
Yield 34%; yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.43 (3H, s), 2.82 (1H, d, J = 10.4 Hz), 3.06 (1H, d, J = 10.4 Hz), 3.73 (1H, dt, J = 2.4, 13.6 Hz), 4.09-4.16 (2H, m), 7.30-7.31 (2H, m), 7.33-7.38 (3H, m), 7.58 (2H, d, J = 8.0 Hz), 7.77 (1H, dd, J = 2.8, 5.6 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.6, 52.4, 52.7, 59.2, 61.4, 106.8, 127.9, 128.3, 128.5, 129.1, 129.6, 132.4, 136.7, 143.7, 148.7, 164.6, 206.5**;** IR (NaCl, neat) *v*: 2976, 1705, 1627, 1351, 1170; HRMS (ESI) calcd. for $C_{22}H_{21}NO_3SNa$ (M^++Na): 402.1140, found: 402.1138.

7-methyl-4-methylene-2-tosyl-2-azaspiro[4.4]non-7-en-6-one (190m)



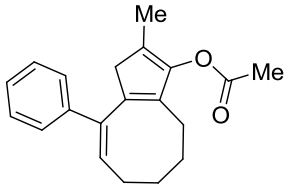
Yield 40%; yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.77-1.78 (3H, m), 2.44 (3H, s), 2.70-2.80 (2H, m), 3.25-3.28 (1H, d, J = 9.6 Hz), 3.45 (1H, d, J = 9.6 Hz), 3.67-3.71 (1H, m), 4.14-4.19 (1H, m), 4.64 (1H, s), 4.89 (1H, s), 7.33-7.35 (2H, m), 7.37-7.38 (1H, m), 7.69-7.71 (2H, m); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 10.5, 21.6, 43.6, 52.6, 56.8, 57.5, 106.7, 128.0, 128.5, 129.8, 130.2, 133.7, 140.7, 144.0, 148.7, 156.8, 206.9; IR (NaCl, neat) *v*: 2971, 1703, 1624, 1353, 1168; HRMS (ESI) calcd. for $C_{17}H_{19}NO_3SNa$ (M^++Na): 340.0983, found: 340.0986.

2-methyl-10-phenyl-7-tosyl-7-azaspiro[4.5]deca-2,9-dien-1-one (190χ)



Yield 40%; yellow solid; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.72 (3H, s), 2.43 (3H, s), 2.71 (1H, d, J = 11.2 Hz), 2.85 (1H, d, J = 19.6 Hz), 3.03 (1H, d, J = 19.6 Hz), 3.33 (1H, dd, J = 8.4, 16.8 Hz), 3.46 (1H, d, J = 11.2 Hz), 4.18 (1H, dd, J = 8.4, 16.4 Hz), 5.88-5.89 (1H, m), 7.02-7.03 (2H, m), 7.19-7.20 (3H, m), 7.33 (3H, d, J = 8.4 Hz), 7.64 (2H, d, J = 8.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 10.4, 21.5, 40.5, 45.6, 52.8, 52.9, 124.0, 127.3, 127.7, 127.8, 128.2, 129.9, 132.5, 138.9, 141.5, 144.0, 157.5, 208.8; IR (NaCl, neat) v: 2971, 1703, 1624, 1353, 1168; HRMS (ESI) calcd. for $C_{23}H_{24}NO_3SNa$ (M^++Na): 394.1477, found: 394.1473.

(Z)-2-methyl-9-phenyl-4,5,6,7-tetrahydro-1H-cyclopenta[8]annulen-3-yl acetate (191δ)



Yield 44%; white solid; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.53-1.63 (4H, m), 1.80 (3H, s), 2.23-2.26 (4H, m), 2.28 (3H, s), 2.81 (2H, s), 5.84 (1H, t, J = 9.6 Hz), 7.21-7.31 (5H, m); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 11.8, 20.6, 21.8, 25.8, 26.1, 27.9, 42.8, 125.5, 126.8, 127.7, 128.1, 128.6, 134.0, 139.0, 140.1, 142.9, 146.4, 168.9; IR (NaCl, neat) v: 2970,

1700, 1627, 1354, 1170; HRMS (ESI) calcd. for $C_{20}H_{22}O_2Na$ (M^++Na): 317.1517, found: 317.1517.

Chapter VII. References

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96. Chan285 (**190χ**) and Chan286 (**191δ**) contain the supplementary crystallographic data for this report. These data can be obtained from Drs. Ganguly or Dr. Li at the Division of Chemistry and Biological Chemistry, School of Physical and Mathematical Sciences, Nanyang Technological University.